“ROLE OF HIGH RESOLUTION ULTRASONOGRAPHY OF PERIPHERAL NERVES IN LEPROSY PATIENTS”

Dissertation Submitted in
Partial fulfillment of the University regulations for

MD DEGREE IN

DERMATOLOGY, VENEREOLOGY AND

LEPROSY

(BRANCH XX)

MADRAS MEDICAL COLLEGE

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI, INDIA.

APRIL - 2017

CERTIFICATE

Certified that this dissertation titled "**ROLE OF HIGH RESOLUTION ULTRASONOGRAPHY OF PERIPHERAL NERVES IN LEPROSY PATIENTS**" is a bonafide work done by **Dr. BALA SOUNDAR V**, Post graduate student of the Department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai – 3, during the academic year 2014 – 2017. This work has not previously formed the basis for the award of any degree.

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DECLARATION

The dissertation entitled "**ROLE OF HIGH RESOLUTION ULTRASONOGRAPHY OF PERIPHERAL NERVES IN LEPROSY PATIENTS**" is a bonafide work done by **Dr. BALA SOUNDAR V** at Department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai – 3, during the academic year 2014– 2017 under the guidance of **Dr. U.R.DHANALAKSHMI M.D., D.D., DNB,** Professor and HOD, Department of Dermatology, Madras Medical College, Chennai -3.

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DECLARATION

I, **Dr.BALA SOUNDAR V** solemnly declare that this dissertation titled "**ROLE OF HIGH RESOLUTION ULTRASONOGRAPHY OF PERIPHERAL NERVES IN LEPROSY PATIENTS**" College during 2014-2017 under the guidance and supervision of **Dr. U.R.DHANALAKSHMI., M.D., D.D., DNB,** Professor and Head of the Department of Dermatology, Madras Medical College,Chennai-600003.

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SPECIAL ACKNOWLEDGEMENT

My sincere thanks to **Prof**. **Dr. M.K. MURALITHARAN., M.S., Mch**., Dean ,Madras Medical College for allowing me to do this dissertation and utilize the Institutional facilities.

ACKNOWLEDGEMENT

I am gratefully indebted to Professor and Head of the Department of Dermatology, **Prof. Dr U.R.DHANALAKSHMI, M.D., D.D., DNB** for her invaluable advice, guidance and encouragement throughout the study. She has been a source of constant motivation and encouragement throughout the study. I am extremely grateful to her for guiding me throughout the study.

I would like to express my sincere and heartfelt gratitude to **Prof. Dr. S KALAIVANI M.D., D.V.,** Director (I/c) and Professor, Institute of Venereology, for her kindness and support throughout the study.

I thank **Prof. Dr. S. KUMARAVEL M.D., DD** Professor of Dermatology for his support and encouragement. I thank my Professor and Head of the department of Occupational and Contact Dermatitis, **Prof. Dr. S. NIRMALA M.D.,** for her help and support. I thank **Prof. Dr .R. PRIYAVATHANI M.D., D.D., DNB., MNAMS.,** Professor of Dermatology for her advice and encouragement. I sincerely thank **Prof. Dr. A.RAMESH, M.D., D.D., DNB (DVL)** Professor of Dermatology for his priceless support. I express my sincere gratitude to **Prof. Dr. V. SAMPATH M.D.**, Professor of Dermatology for his guidance and support. I am grateful to **Prof. Dr. J.MANJULA M.D., DNB.,** Professor, Department of Dermatology for her invaluable guidance and help.

.I wish to thank **Prof. Dr.. K. MANOHARAN.M.D.,D.D.,** former Professor and Head of department, Dermatology for his support and motivation.

I humbly thank **Prof. Dr. C. JANAKI M.D., D.D**., former Professor of Dermatology for her priceless support.

I also wish to thank **Prof. Dr. V.SUDHA M.D., D.V., D.D.,** former Professor and Director, Institute of venereology for her support and motivation.

I wish to thank **Prof .Dr. THILAGAVATHI., MD., DV**former Professor and Director, Institute of venereology for her support.

I humbly thank my Co-Guide **Prof. Dr. S. Kalpana M.D. (R.D)**, Professor of Radiodiagnosis for her valuable guidance throughout my work. I humbly thank my Co-Guide, **DR. R. MANIPRIYA MD (DVL)., DCH**., assistant prof. of dermatology for her valuable guidance throughout my work. I would like to express my sincere and heartfelt gratitude for the time which she has devoted for my research project.

I extend my gratitude to **Dr. R. MADHU M.D., D.C.H., Dr. V.N.S. AHAMED SHARIFF M.D.D.V.L., Dr. SAMUEL JEYARAJ DANIEL M.D. D.V.L., Dr. B VIJAYALAKSHMIM.D. (D.V.L.) , Dr. K. UMA MAHESHWARI M.D.D.V.L., DR K DEEPA MD (DVL)., , Dr. C.L. CHITHRA MD (DVL),** Assistant professors, Department of Dermatology for their kind support and encouragement.

I also thank my Assistant Professors **Dr. P. PRABHAKAR M.D.D.V.L., Dr. C. VIDHYA, M.D.DVL., Dr. R HEMAMALINI M.D.D.V.L., Dr H.DHANASELVI M.D (DVL)., DLO., Dr. K GAYATHRI M.D.D.V.L., Dr. E. BALASUBRAMANIAN M.D.D.V.L., Dr. S. SNEHAVALLI M.D.D.V.L.**, of Institute of Venereology for their able guidance.

I express my thanks to **Dr. G.K. THARINI M.D., Dr. N. SARAVANAN M.D. D.V.L., Dr. NITHYA GAYATHRI DEVI, M.D.D.V.L.**my former assistant professors, Department of Dermatology, for their support and help.

I wish to thank to **Dr. P.MOHAN M.D., D.V., Dr. S. VENKATESAN D.V., DNB (D.V.L.), Dr. V. GOMATHY M.D. D.V.L** former Assistant Professors, Institute of Venereology for their constant guidance.

I am thankful to my colleagues for their support throughout the study. I am also grateful to all paramedical staffs for rendering timely help to complete my study. I am also extremely thankful to my family for their motivation and encouragement.

Last but not the least I am profoundly grateful to all patients for their co-operation and participation in this study. They have been the principal source of knowledge which I have gained during the course of my clinical research.

CONTENTS

ABBREVIATIONS

- HRUS – High resolution ultrasonography
- CD - Colour Doppler
- CSA – Cross sectional area
- US- Ultrasound
- MRI – Magnetic Resonance Imaging
- RLN – Recurrent Laryngeal Nerve
- AFB – Acid Fast Bacilli
- HBV – Hepatitis B virus
- WHO – World Health Organisation
- TT - Tuberculoid leprosy
- BT - Borderline tuberculoid
- BB - Borderline borderline
- BL - Borderline lepromatous
- LL -Lepromatous leprosy
- PNL – Pure Neuritic Leprosy
- AIDS – Acquired Human Immunodeficiency Syndrome
- KDa – Kilo Dalton
- MHz - Megahertz
- FNAC – Fine Needle Aspiration Cytology
- PGL – Phenolic glycolipid

- HLA – Human Leukocyte Antigen
- DNA – Deoxy ribonucleic acid
- MAP – Mitogen Activated Protein kinase
- TGF - Transforming Growth Factor
- IFN – Interferon
- TNF – Tumour necrosis Factor
- iNOS – Inducible Nitric Oxide Synthase
- PCR – Polymerase Chain Reaction
- USG –Ultrasonogram
- ND-O-BSA – Natural Disaccharide O linked Bovine serum Albumin
- NT-O-BSA - Natural Trisaccharide O linked Bovine serum Albumin
- VMT – Voluntary muscle testing
- NCS – Nerve conduction studies
- MRC- Medical research Council
- NFI – Nerve function impairment

INTRODUCTION

Leprosy is an infectious disease caused by Mycobacterium leprae, an intracellular acid fast organism predominantly found in macrophages of skin and schwann cells of peripheral nerves.[1] Leprosy affects skin and nerves mostly. Involvement of latter is of importance as it leads to disability. Prompt recognition and early treatment prevents occurrence of disability. It can affect any system in the body except brain and spinal cord.

In early 1860's, Henry Vandyke Carter stated that "leprosy is probably the only disease known which is confined to the peripheral nerves and the sentient skin". He made a note that nerve involvement and enlargement followed a pattern not in random .[2]

Leprosy is a disease of social importance and stigma because of its disability and deformities on chronic course. Diagnosis of leprosy can be easy most times through presence of more than one out of three cardinal signs as recommended by WHO expert committee on Leprosy. Sometimes, presence of only one of these feature causes diagnostic difficulty and necessitate further investigations.

Mycobacterium leprae is the only bacterium known to affect myelination and cause peripheral neuropathy. Nerve damage affects

mainly the ulnar, median, lateral popliteal and posterior tibial nerves resulting in characteristic nerve enlargement[3,4]. Normally, assessment of nerve thickening is done clinically which is very subjective. Using high resolution ultrasound, objective measurement could be done. It is also possible to pick up reactions early on visualization of blood flow by Colour Doppler imaging of the peripheral nerves vascularity[5].

Efforts to diagnose early or subclinical neuritis could ameliorate the nerve damage which leads to functional impairment of limbs, ulcer formation and stigmatizing deformities. Early detection of nerve involvement at the time of diagnosis or during a leprosy reaction is important so that adequate treatment can be started and further nerve function impairment can be prevented.

Mycobacterium leprae is an acid-fast, slow growing bacilli. It prefers cooler temperature for growth. It can remain dormant in certain tissues and causes relapse. It cannot be grown in artificial media.

Leprosy presents as a spectrum of disease with varying manifestations depending upon the host immune response. Nerve damage is seen throughout the spectrum.

REVIEW OF LITERATURE

CLINICAL FEATURES

Leprosy is a spectral disease. The clinical presentation varies from few to widespread lesions[7].

A case of Leprosy is defined as an individual who has not completed the course of treatment and has one or more of the three cardinal signs[8]:

1) Hypopigmented / Erythematous skin lesion with definite loss or impairment of sensation
2) Involvement of the peripheral nerves - definite thickening with sensory impairment.
3) Positive AFB Slit Skin Smear.

In 1962 and 1966[9,10], Ridley and Jopling proposed a new classification based on the clinical features , histopathology, bacterial load and the degree of cell mediated immune response (CMI) against M.leprae[7]. This classification is most widely used.

Based on these immunopathological criteria, patients are divided into a five- group spectrum[7]

1) Tuberculoid leprosy (TT)
2) Borderline tuberculoid (BT)
3) Borderline -borderline (BB)

4) Borderline lepromatous (BL)

5) Lepromatous leprosy (LL)[11]

Pure neuritic leprosy (PNL) and Indeterminate leprosy are not included in this classification.

STRUCTURE OF NERVE:

Peripheral nerve is composed of two cellular elements – Neuron and Schwann cell[12, 13].

Neurons are the structural and functional unit of the peripheral nerve. It contains a cell body, dendrites and an axon. Axon is unbranched for a long length and branches at the end of its process. Multiple axons are grouped together to form a nerve fascicle. Many fascicles are grouped into peripheral nerve.

Axons are long tubular process surrounded by endoneurial connective tissue. Perineurium, a dense connective tissue covers each fascicle. Perineurium is made of multiple perineural cells, Type I and II collagen fibres and elastic fibres in circumferential, oblique and longitudinal direction. Perineural cells have a basal lamina containing laminin and fibronectin. The bridges between the perineural cells maintains the blood nerve barrier and preserve endoneurial environment. Epineurium consist of type I and III collagen fibrils, fibroblasts, elastic

fibres and mast cells. It remains intact, even if axons are damaged and provide path for nerve regrowth. Interchange of axons between fascicles takes place and minimises functional deficit when nerve damage occurs[14].

Axons terminate as sensory nerve ending in skin. After repeated division and reunion, fascicles produce nerve plexus along the course resulting in sensory, motor and mixed nerve.

Schwann cells of unmyelinated axon do not have lysosomes. This facilitates its survival and numerous bacilli are found in these nerves. Myelination thus protects the axon and helps in rapid impulse transmission.

Vascular Supply

Extensively interconnected microvascular systems ensure adequate vascularization of the peripheral nerves. Intraneural microvessels extend longitudinally within the epineurium, with this system being reinforced by extrinsic segmental regional blood vessels[13]. Blood vessels in the nerve are enclosed in connective tissue sheath. Vasa nervorum enter the epifascicular epineurium and travels in interfascicular epineurium and divide into arterioles. These penetrate the perineurium in oblique manner and enter endoneurium which further divides into capillaries with tight endothelial junction forming a barrier.

Veins from the nerves drain blood to the heart.

Lymphatics are absent in endoneurium and perineurium and present only in epineurium.

There are three different types of nerve fibers – motor, sensory and sympathetic. Sensory and motor nerves contain both myelinated and unmyelinated nerve fibers. The postganglionic sympathetic nerves containing unmyelinated fibers innervate the skin, blood vessels and hair follicles[13].

Nerve fibres are classified according to their conduction velocities which in turn are directly related to the size of the fibres and myelination[15].

- A and B fibres are myelinated and carry impulse quicker.
- C fibres are unmyelinated and conduct slower.
- A α and A β fibres are motor to skeletal muscles and also carry proprioception.
- A β fibres carries touch, vibration and pressure sense from skin.
- A δ fibres are sensory and carries pressure, temperature and nociception from skin.
- C fibres carries pain, temperature and pressure sensation.
- A δ and C fibres are called as small diameter afferent fibre .

- A β fibres are called as large diameter afferent fibre.

On histological examination, nerves look as wavy structure with slender schwann cell nuclei. Axons and myelin need special stain like silver impregnation and Solochrome cyanine stain.

Functions-

- Nerve fibres are responsible for conducting impulses to and from the peripheral organs.
- Perineurium has important barrier functions, protecting the fascicle from interfascicular tissue fluids and from infection[13].

NERVE INVOLVEMENT AND COMPLICATIONS:

Mycobacterium leprae frequently invades cutaneous nerves and peripheral nerve trunks .The outcomes of this invasion depends on

- Nerves affected
- Host immunological response
- Type of leprosy
- Reactions

Peripheral nerves affected in leprosy

1. Supra orbital nerve

2. Facial nerve

3. Great auricular nerve

4. Supra clavicular nerve (rare)

5. Radial nerve

6. Ulnar nerve

7. Radial cutaneous nerve

8. Median nerve

9. Femoral cutaneous nerve (rare)

10. Lateral popliteal (common peroneal) nerve

11. Superficial peroneal nerve

12. Sural nerve

13. Posterior tibial nerve

Nerve damage usually results in[7]:

- Sensory damage[16, 17]

  Impairment or complete loss of sensation in the areas of peripheral nerve distribution. Nerve damage may occur at the level of skin or subcutis and also at the level of the nerve trunks.

- Autonomic and motor damage[16, 17]

  Autonomic damage causes cyanosis, dryness and reduction or absence of sweating in the affected areas . Paresis or paralysis and atrophy of muscles occur .

The most frequently affected peripheral nerves (symmetrical or asymmetrical) in leprosy patients are

ULNAR NERVE:

The most frequent site of damage is proximal to olecranon groove resulting in loss of sensation and progressive muscle atrophy over hypothenar eminence. Little and ring finger affected resulting in minimal or ulnar claw. In the absence of treatment, disabilities, ulceration, bone involvement and loss of digits are noted in late stage [7,16,17,18,19].

MEDIAN NERVE:

It is affected either at antecubital fossa (bend of elbow) or proximal to carpal tunnel. Most frequently damaged at the carpal tunnel area resulting in sensory and autonomic disturbance over radial half of the hand and paralysis of thenar eminence and first two lumbricals. Hand and thenar eminence becomes flat. Thumb cannot be abducted or opposed. Median and ulnar nerve damage occurring together gives rise to total claw hand[7,16,17,18,19].

RADIAL NERVE[7,16,17,18,19]**:**

Radial nerve is damaged at upper arm usually. Severe damage results in wrist drop and sensory loss over dorsal and medial region of hand. Radial nerve damage is usually uncommon.

COMMON PERONEAL NERVE:

Common peroneal nerve is frequently affected in popliteal fossa/ around the neck of fibula. Dorsiflexion and eversion of foot are affected initially. In later stage, there is hypotrophy of tibialis anterior, foot drop, high stepping gait, hyperkeratosis, ulceration and infection of lateral surface of plantar area. This is described as perforating plantar disease. Lateral side of the leg, dorsum of foot and lateral plantar surface may show sensory loss and autonomic disturbances.

POSTERIOR TIBIAL NERVE:

Posterior tibial nerve is damaged frequently proximal to the area around medial malleolus. Paraesthesia and anaesthesia of sole, loss of sweating, hyperkeratosis, ulceration, infection, osteomyelitis, clawing and loss of toes leads to severe disabilities[7,16,17,18,19].

FACIAL NERVE :

Temporal and Zygomatic branches can be affected. Lagophthalmos is a frequent and serious complication. In advanced stage, buccal, mandibular and cervical branch are also affected resulting in loss of facial expression and difficulty in closing mouth.

Differential Diagnosis Of Nerve Involvement[7,21]

- Polyneuropathy associated with AIDS
- Déjérine-sottas's disease
- Diabetes
- Amyloidosis
- Systemic lupus erythematosus
- Systemic scleroderma
- Neurotoxicity associated with drugs (isoniazid, poisoning with arsenic,

  Mercury, thallium and others)
- Nerve compression (carpal tunnel syndrome, cervico-brachial syndrome and others)
- Neurogenic muscular atrophy (TOOTH-CHARCOT-HOFFMAN)
- Hereditary sensory neuropathy (Thevenard's Syndrome),
- Syringomelia

Neurological complications of leprosy causes immense stigma and concern for the patient. Leprosy has always been misdiagnosed particularly in non-endemic areas. Patients with deformities and sensorimotor deficits may attribute their symptoms to vascular/ neurological diseases. Therefore it is essential that, the treating physician should know about different neurological presentation of the leprosy and make accurate diagnosis clinically.

Two distinctive features of Mycobacterium leprae is accountable for its characteristic clinical features are [22]:

1) Ability to invade Schwann cells of peripheral nerve
2) Requiring optimum temperature in the range of 28-32 º C for its optimum growth.

Bacilli multiply in cooler tissues of the body mainly in the skin, testes and anterior segment of eye.

Nerve damage in Leprosy occurs in three ways[22]

1) Destruction of intra cutaneous nerve
2) Involvement of peripheral nerve trunk in cooler and superficial location
3) During reactional state in the chronic course of disease.

Temperature linked pattern of sensory loss is specific for leprosy[23]. This feature helps in distinguishing leprous neuropathy from other neuropathies. Sensory loss is one of the cardinal symptom before the other evidence of the disease. Sensory abnormalities precede the motor involvement in all spectrum of leprosy. Temperature, pain and touch are affected in this order[24]. Proprioception and vibratory sensation are usually normal until the late stage of disease. The affected nerves become thick, hard and sometimes visible.

Type of leprosy determines evolution, pattern and extent of sensory deficits and motor paralysis.

Tuberculoid leprosy :

Nerves are involved by extension of infection from cutaneous nerve branches. Nerve damage is asymmetrical, patchy and often unilateral. Skin lesions are few in number up to three, that may show sensory loss which is sharply delineated.

Nerve damage occurs as a result of host immune response to the bacilli and is not due to massive proliferation of bacilli[25]. Nerve trunk underlying the patch may be affected[26].

The major sensorimotor nerves affected are ulnar, median, peroneal and facial nerve. The commonly affected sensory nerves are

superficial radial cutaneous nerve, digital nerve, posterior auricular nerve and sural nerve. When the response of the host to the bacilli is intense, it results in necrosis with cold nerve abscess formation.

Lepromatous leprosy:

Skin lesions are numerous, widely disseminated and symmetrically distributed. It may be macules, papules, nodules or plaques. Edges are indistinct, surface is shiny. Early skin lesions show normal sensation. Loss of sensation is not sharply defined as in tuberculoid leprosy. Even though the nerves are enlarged, it functions normally. In the initial stage itself, numerous bacilli may be seen in the nerves but minimal sensory loss seen due to poorer host immune response . M.leprae produces a unique pattern of neurologic deficits since it reproduces in cooler areas of the skin. Low resistance on host side favours hematogenous dissemination causing symmetric neurological deficits.

Temperature linked sensory loss pattern of LL type can be easily distinguished from classical “glove and stocking” anaesthesia of other peripheral neuropathies.

Sensory deficits

Sensory loss is usually symmetrical .Sensory loss begins from the ear and then to the dorsum of hand and forearm, dorsum of feet,

anterior and lateral part of the legs. With the progress of disease, sensation lost over dorsal forearm, medial legs, elbows and knees. Nose, cheeks, central abdomen, breasts and `buttocks are affected then. Sparing of palms and soles are seen at this stage due to warmth provided by the insulating effect of thick cuticle. Complete insensitivity of palms occurs in later stage. Similarly from lower extremities sensory loss extends over to abdomen with some islands of normal sensation[22]. Axilla, perineum, groin, popliteal fossa, sternal area and longitudinal strip of area extending from intergluteal cleft to central back are spared which are considered to be the "immune zones in leprosy".

Motor deficits

Motor fibers that are close to the skin are most affected. Ulnar nerve and lateral popliteal nerve affection leads to clawing and foot drop. Posterior tibial nerve involvement in lower third of leg causes atrophy of intrinsic muscles of foot. Ulnar and median nerve innervated hand muscles shows atrophy. Radial nerve motor deficits are less common in LL.

Autonomic deficits

Autonomic fibres are also affected along with sensorimotor fibres. Loss of sweating occurs over insensitive areas. Extremities are cold and

dusky. Autonomic functions like postural hypotension, nocturnal diarrhoea, abdominal crises, bladder dysfunction and impotence are not affected in leprosy.

Cranial nerves involvement

Facial and trigeminal nerves are most affected. Involvement of vestibulocochlear, glossopharyngeal, vagus and spinal accessory nerve have also been reported.

Facial nerve involvement is patchy and bilateral. Its branches over forehead, zygomatic process and mandible which are close to skin are affected. Weakness in closing eyelids is first seen. Progressive deterioration causes lagophthalmos and entropion which results in inward turning of eyelashes and corneal abrasion and ulceration. Orbicularis oris, superficial muscles of nasolabial fold and frontalis muscle are also affected.

DIMORPHOUS LEPROSY/BORDERLINE LEPROSY

Importance of this spectrum is because of increased frequency of nerve involvement and reactions leading to disabilities and deformities. It is unstable in nature and features both forms of leprosy. Reactions are more common and vulnerability of nerve damage is more [28].

Borderline tuberculoid shows enlarged nerves in an asymmetrical pattern. Nerve damage resulting in anaesthesia or motor disturbance is seen at presentation.

The most striking feature is increased susceptibility to type 1 reactions in both skin and nerves. Nerves are tender and show functional deficits. If untreated at this stage, progressive damage and deformities occur.

Mid-borderline leprosy is highly unstable either downgrades to BL or upgrades to BT leprosy. Skin lesions are multiple with tendency towards symmetry. Annular, geographic lesions and inverted saucer shaped lesions are seen. Many nerves are involved but are not symmetrical as in LL. Nerve damage is variable. Symmetrical peripheral sensory loss is unusual.

Borderline lepromatous leprosy shows numerous skin lesions varying from macules, papules, plaques and nodules with tendency towards symmetry. Face and ears show infiltration. Peripheral nerve trunks are thickened but lack symmetry. Nerve damage is less frequent than BT and BB. Increased susceptibility to type 2 reaction is seen.

POLYNEURITIC LEPROSY[29]

It is characterised by absence of skin lesions but sensory loss is seen over the area of distribution of involved nerve with or without motor loss. In some of these cases, dermal lesions appear later during the course. It accounts for 5-10% of all leprosy patients. Clinical presentation may be in the form of mononeuritis or mononeuritis multiplex. The most commonly involved nerve is ulnar nerve. Both BT and BL forms have been seen in this type. Diagnosis is confirmed through nerve biopsy. FNAC of nerve has been helpful as less invasive procedure and alternative for biopsy.

Pathomechanism of nerve damage

Peripheral neuropathies are caused by number of etiologies such as nutritional, genetic or hereditary, metabolic, malignancy, toxins, infections, which affects axons and Schwann cells.

It manifests clinically as disturbance in sensory, motor, reflex function and autonomic dysfunctions. Along with these features, there may be coexisting thickening of peripheral nerves clinically.

Functional deficits are usually distal and symmetrical. It begins as mononeuritis multiplex then evolves into polyneuropathy.

When small nerve fibres are affected, pain and temperature sensation are affected whereas large fibres involvement causes areflexia, sensory ataxia and minimal cutaneous sensory deficits.

- Fusiform thickening is seen in leprous neuropathy
- Beaded thickening is seen in Amyloid neuropathy
- Uniform thickening is observed in Hereditary neuropathy
- Thickening of peripheral nerves are also seen in persons with heavy manual work and generalised muscular built such as wrestlers and weight lifters.

In Leprosy, small nerve fibres are affected predominantly. Sensory modalities are lost in the following sequence[30]:

Temperature → Touch→ pain→ pressure

Hansen disease neuropathy is primarily demyelinating but usually results in axonal loss during its course. The most affected nerves are in the distal limbs and in osseofibrous tunnels.

Three types of damage to nerve structures recognised in leprosy are[33] :

- Wallerian degeneration
- Distal axonopathy
- Demyelination

- **Wallerian degeneration :**

Crush or transection injury to axon leads to fragmentation. This causes nerve segment distal to injury to be degenerated. It is seen in toxic and metabolic neuropathy. Recovery takes more time.

- **Distal axonopathy:**

Axonal degeneration and demyelination begins in the most distal part of neuron followed by axonal death in retrograde progression. This accounts for characteristic (Glove and stocking) distal sensory loss.

- **Demyelination :**

Segmental demyelination of axons occur leading to decreased conduction velocity and slow generation of action potential leading to conduction block. Schwann cell show proliferation along the peripheral nerves which are arranged concentrically forms lamellated structure. This causes induration and enlargement. Recovery time is less in demyelination type of nerve damage.

Seddon divided nerve injuries by severity into three broad categories[32,34]

- **Neuropraxia:**
    - It is the mildest form of nerve injury.
    - Physical continuity of the nerve is preserved.

- **Axonotemesis:**
    - It is the more severe form of injury.
    - Axons are severed with preservation of neural connective tissue.
- **Neurotmesis:**
    - It is the most severe form of nerve injury.
    - Axons and myelin sheath along with connective tissue component are damaged.
    - Axonal regeneration is blocked by fibrosis.

Three phases of evolution of leprous neuropathy:

1) Infection of schwann cells by Mycobacterium leprae - Clinically asymptomatic or mild disease
2) Acute and subacute episodes of reactions interrupting chronic disease. Symptoms are severe with motor and sensory defects
3) Fibrosis of nerves leading to interstitial neuropathy.

Entrapment neuropathy and neuropathic pain are the two complications develop during disease.

Neurotropism of Mycobacterium leprae:

1) Specific binding site for Mycobacterium leprae at α-dystroglycan in G domain of α2 chain of laminin in basal lamina of Schwann cell in axon unit[35].
2) Multiplication is more at temperature 10º c lower than our body temperature.

Sensory deficits first occur on cooler parts of the body in Lepromatous leprosy. Warmer parts of body such as scalp, anterior neck, sternum, perineum, intergluteal folds, antecubital and popliteal fossa and toe webs. Skin over paraspinal muscles is spared.

Deep tendon reflexes are usually preserved in Lepromatous Leprosy. This differentiates it form other causes of neuropathy.

Peripheral nervous system is made to function normally through balance between two functions of immune system

1. Protection from infection
2. Aid in nerve regeneration and physiology after injury

Special features of nerve damage in Leprosy:

- Central Nervous System is unaffected
- Sensory fibre involvement is a key feature
- Thickening is maximum at superficial location
- Interfascicular plexus aids in nerve damage

Dehio postulated that leprous neuropathy is an ascending neuritis with centripetal spread of damage. Motor nerve fiber involvement occurs as a result of lateral spread in mixed nerve[36].

Khanolkar et al[37] inferred that the bacilli multiply favourably within the schwann cells of axon. Non myelinated fibre schwann cells are strikingly involved[38,39].

Other contributory factors which accelerate nerve damage:

- Interfunicular plexuses serves as preformed pathway for spread of bacilli[40].
- Intraneural inflammation and intraneural edema
- Unyielding epineurium causing damage by compression of nerve fibres.
- At osseofibrous tunnel, swollen nerve trunks are further compressed such as median nerve at carpal tunnel.
- Tissue anoxia / hypoxia results from compressed perineural arteries[41].

ENTRY OF M.leprae:

M.leprae gains entry into the peripheral nerve through two main routes

1) via bloodstream- enters endoneurium through monocytes and vascularized endothelial cells[42,43,44]

2) via schwannian relay- distal sensory schwann cells and spread from one cell to another along the Schwann cell column[45,46].

Neural preference of bacilli is further supported by cooler temperature, trauma to nerves resulting in damage to capillaries and increased bacterial adhesiveness[47].

Absence of lymphatic channels in the endoneurium, tight junction between endothelial cells and also tight junction between perineural cells favours and secures the bacilli from immune surveillance. These two specialized barrier also prevents the entry of drugs into nerve and reduces the effectiveness of treatment[47,48].

Poor antigen presenting capacity of schwann cell along with poorly equipped killer enzymes makes Schwann cells ideal site for survival, proliferation and depository for M.leprae[49].

Infection of Schwann cell:

Adhesion and invasion of Schwann cell by M.leprae have been studied through several in vivo studies[50].

M.leprae binds to the G domain of α 2 laminin present on the surface of Schwann cells through its receptor present on cell wall 21k Da histone like protein[51].

Similarly, PGL-1, a surface M.leprae specific antigen binds to laminin 2 and helps in invasion.

α 2 laminin and dystroglycan α6β4 integrin largely restricts the leprosy infection to peripheral nervous system. Since these two molecules are absent in the Central Nervous System[52].

M. leprae infected schwann cells shows loss of their ability to proliferate and synthesise DNA[53].

Degeneration of nerves in leprosy:

It depends on type of leprosy, bacillary load duration of disease. Segmental demyelination is predominantly seen in lepromatous lesions. Wallerian or axonal degeneration is seen in tuberculoid type of lesions. Demyelinating lesions dominates the entire spectrum of leprosy. Regeneration and remyelination changes also occur during the course[54].

Two distinct types of demyelination in leprous neuropathy are

1) Secondary demyelination- results due to axonal component atrophic changes
2) Primary Segmental demyelination[55] :

- Occurs at site of inflammation
- Attributed to direct myelinolytic action of inflammatory infiltrate.

The final result of these processes culminates in severely damaged nerve with loss of nerve fibres and substitution with connective tissue and fibrosis.

Immunological aspects of nerve damage:

The host's immune response play crucial role in causing variety of structural and functional changes that represent leprosy. Both cell mediated immunity and humoral immunity plays a role.

Cell mediated immunity predominates in tuberculoid and borderline tuberculoid form. Humoral immunity predominates in lepromatous and borderline lepromatous form. Both Cell mediated immunity and humoral immunity together plays in Borderline forms of Leprosy.

Protective immunity in leprosy is executed through HLA gene complex, especially HLA-DR2 loci[56].

Autoimmune type of damage:

Damaged leprosy nerves release auto antigens that later sensitise and causes nerve damage even without the bacilli or inflammatory cells[57].

Myelin proteins are released which when exposed to immune system, auto sensitisation occurs. Demyelinating antibodies are present in the serum of patients. These antibodies are produced secondary to damage to nerves. They do not play primary role in nerve pathology[58].

Role of M.leprae antigen:

Nerve damage continues to occur even after effective killing of M.leprae bacilli through multidrug therapy. Persistence of M.leprae antigen in the skin and nerve lesions are seen in biopsy specimen in both tuberculoid and lepromatous spectrum patient[59,60,].

These antigens can cause cell mediated hypersensitivity and dysregulation of MAP kinases and dephosphorylation of neurofilament proteins[61,62] .

Role of cytokines in nerve damage:

Inflammatory cells in the lesions are associated with release of different tissue destroying cytokines.

TGF-β is one of major cytokine involved. It plays important role in pathogenesis. It is an immunosuppressive cytokine and its level increases form tuberculoid pole to lepromatous pole[63]. It also plays role in entry, replication and persistence of M.leprae in host. It causes downregulation of TNF- α and IFN- γ and inhibits inducible NOS (iNOS) synthase by macrophages and favours bacterial replication[64].

Insidious nerve damage:

Dysfunction of nerves in leprosy is painless and slowly progressive frequently. Even the patients are unaware of these dysfunction.

ASSESMENT OF NERVES IN LEPROSY

1. **Clinical assessment**
2. **Neurophysiologic assessment**

   Nerve conduction studies
3. **Radiological assessment**

   Ultrasound examination and Magnetic Resonance Imaging

CLINICAL ASSESSMENT:

It is routinely used method of evaluation.

1. Palpation of peripheral nerves
2. Grading of nerve thickening , tenderness and pain
3. Assessment of Nerve function impairment (NFI)

a. Sensory NFI through Semmes Weinstein monofilaments
b. Motor NFI through Modified MRC scales for VMT
c. Autonomic NFI through sweat test

Sensory evaluation:

Sensory examination is essential in patients with leprous neuropathy as sensory loss almost always precedes motor loss. The pattern of sensory loss is highly suggestive of leprosy are[31]

1) It occurs in cooler regions of the body
2) Patchy distribution early then in the peripheral nerve trunk distribution
3) Pain and temperature sensation more involved.

Graded sensory testing is a very sensitive tool to supervise the sensation and guide for patient care[31].

Nylon monofilaments testing is useful in follow up of leprosy patients.

Motor function testing:

It is done through voluntary muscle testing (VMT) using British Medical Research Council (MRC) scale grading [31,65].

Grade 5: Normal power with full resistance

Grade 4: Muscle contraction against slight resistance but subnormal power

Grade 3: Movement possible without resistance

Grade 2: Active movement when gravity is eliminated

Grade 1: Flicker of movements

Grade 0: No movement

Each muscle is tested manually and assessed for motor function using MRC scale. For each nerve, at least two muscles should be tested.

Palpation of Nerve[31]:

It is done for assessment of thickness, tenderness, pain , consistency, presence of irregularities or nodularities, abscess etc.

Significant inter-observer variation may exist but good intra-observer correlation[66].

Nerve enlargement is the most frequent finding. Nerves are palpated at their most superficial locations.

Grading for thickening:

Grade 0 - No nerve thickening
Grade 1- Thickened compared to the opposite side
Grade 2- Rope like thickening
Grade 3 : Beading or nodularities of nerve

Grading of nerve tenderness

Grade 0 – No pain on palpation even when asked about it
Grade 1 - painful on palpation when asked about it
Grade 2- winces with pain during palpation
Grade 3 : withdraws the limb on palpation

Autonomic function testing

It is tested through pharmacological tests like Histamine test and Starch iodide test [67,68,69].

Neuropathic Pain[70]:

Visual Analog Scale for neuropathic pain

For assessment of pain, it is used. This includes grading from 0 to 10.

0 means no pain

10 means unbearable incapacitating pain

It has the limitations of being very subjective.

DIAGNOSIS OF LEPROSY

Leprosy is diagnosed mostly through clinical examination. Diagnosis of leprosy is made through following methods:

- Clinical diagnosis
- Laboratory Diagnosis
- Serological Diagnosis

An astute leprologist can diagnose leprosy by clinical examination alone. Danger of diagnostic delay happens with atypical presentations. Laboratory method plays a major role in early diagnosis and monitoring of response to treatment.

LABORATORY DIAGNOSIS:

1) Slit skin smear

In 1927, Wade and Rodriguez first developed Slit Skin Smear technique. It was further standardised by Cochrane in 1947. International Federation of Antileprosy Associations (ILEP) elaborated more about this method[71].

Role of slit skin smear examination[72]:

Slit skin smear examination serves the following purpose:

1) To confirm the diagnosis of leprosy
2) To classify the disease
3) To determine the disease activity
4) To assess the progress
5) To follow up the patient on treatment

Indication for slit skin smear:

Sites:

Currently Slit Skin Smear are taken from four sites

1) Right earlobe
2) Forehead
3) Chin
4) Left buttock in men
5) Left upper thigh in women

It is also taken from suspicious lesion if present.

In Borderline Lepromatous Leprosy, eight smears are taken which includes four active lesions and four routine sites, as the bacterial load varies in different site.

Smears made are stained by Modified Ziehl Neelson method and examined using light microscope under oil immersion objective

The number of Acid Fast Bacilli in each oil immersion field is counted and graded. Live and dead bacilli are made out through morphology of the bacilli[72].

Ridley defined a method of assessment of Bacterial index. It is universally accepted method for determining the bacterial load in leprosy patients. It is graded as

6+ >1000 bacilli and globi in an average microscopic field

5+ > 100 bacilli in an average microscopic field

4+ > 10 bacilli in an average microscopic field

3+ 1-10 bacilli in average microscopic field

2+ 1-10 bacilli in 10 microscopic fields

1+ 1-10 bacilli in 100 microscopic fields

0 No bacilli after searching at least 100 minimum fields

Morphological Index[73]:

It is the percentage of solid staining bacilli present after calculating 200 bacilli lying singly.

Nasal mucosal smear[74]

Involvement of nasal mucosa is 100 % in lepromatous leprosy patients. Nasal smears helps in diagnosis and assessing the response of the patient to treatment and his infectivity.

Skin biopsy[75]**:**

It is invasive technique and needs technical expertise .

Stains used :

1) Hematoxylin and Eosin
2) Job Chacko modification of Fite Faraco stain[76]
3) Gomori's Grocott Methanamine Silver stain
4) Fluorescent microscopy to detect Mycobacterium leprae
5) Immunohistochemical staining using Mycobacterial antibodies
6) In situ hybridization and PCR
7) S-100 stain for Schwann cells

Nerve biopsy:

Thickened sensory nerve is selected for biopsy. It is useful in confirming diagnosis of leprosy particularly in patients with pure neuritic leprosy.

Sensory loss resulting from the procedure is minimal[77].

Suitable nerves:

- Sural nerve
- Radial cutaneous nerve
- Superficial peroneal nerve
- Cutaneous nerve of forearm or thigh
- Supraclavicular nerve or greater auricular nerve
- Supraorbital branch of fifth cranial nerve

Stains used

- Fite Faraco for AFB in nerve
- Luxol fast blue stain for myelin[78]
- Bodian stain for axons[79]

FNAC:

- FNAC is simple and effective diagnostic method.
- It can be done in an office setting.
- USG guidance can be sought for deeper pathologies.
- Aspirates obtained contains cellular material with numerous foamy macrophages and a few mononuclear lymphocytes in lepromatous leprosy
- It is also useful in studying lymph nodes in LL and diagnosis of pure neuritic leprosy.

Serological and molecular diagnosis:

Serodiagnosis:

- M.leprae specific lipid antigen- PGL-1 (Phenolic Glyco Lipid-1) on Mycobacterium leprae cell wall forms the basis of test.
- ND-O-BSA/NT-O-BSA in ELISA for diagnosis of leprosy[80,81].

Gene amplification Techniques [82,83]:

- Conventional DNA based PCR
- Nested PCR
- Reverse Transcriptase PCR
- In situ Hybridisation and in situ PCR
- Real time PCR

NEUROPHYSIOLOGICAL STUDIES[31]:

The electrophysiological testing of nerves forms a major part in assessment due to its specificity to nerve function.

Nerve conduction studies and needle electromyography are included in this. It provides information on

- Nerve involvement
- Its primary pathology- demyelinating or axonal
- Its temporal profile[84]

The sensitivity of Nerve conduction study in leprosy is 88% but abnormalities are not specific to Hansen neuropathy[85]. The main parameters found are conduction velocity, latency, amplitude and area of response.

Abnormalities can be detected even when nerves are not clinically involved. Patients with Nerve conduction studies abnormalities are more liable to develop reactions and neurological impairment.

The classic pattern of abnormality seen in sensorimotor asymmetric polyneuropathy with focal demyelination and distal axonal impairment[86].

It is useful in diagnosis of pure neuritic leprosy and selecting the site for nerve biopsy[87, 88].

Needle electromyography:

It is a useful method to detect motor axonal involvement and gives data on temporal profile as lesions. It is an important adjunct to nerve conduction studies.

Limitations:

- Differentiation between demyelination and axonal lesion is difficult sometimes.

- Abnormalities seen are not specific to leprosy and cannot directly diagnose leprosy.
- Evaluation of small cutaneous nerves are not possible
- Small nerve fibres affected early in disease cannot be assessed[89].

Advantages:

- More specific to nerve function
- Helps in diagnosis of pure neuritic leprosy
- Useful in follow up of patients and to find out the effectiveness of therapy
- For assessing type 1 and 2 reactions[31]
- Early detection of new nerve lesions[31]
- Identifies the entrapment nerve lesions

IMAGING IN LEPROSY:

Besides clinical and neurophysiological assessment, peripheral nerve imaging is a vital component in the evaluation of peripheral nerve. Two modes of imaging used are USG and MRI.

USG imaging is the first choice of technique for assessing peripheral nerves, due to its low cost and wide availability . It is non-invasive too. Dynamic imaging is possible. Entire course of nerve is evaluated during single examination. But needs expertise and anatomic competence.

High Resolution Ultrasonography of peripheral nerves is a relatively novel imaging field.

In 1985, Solbiati et al, studied Recurrent laryngeal nerve (RLN) by sonography[90].

In 1988, Fornage first reported the possibility of peripheral neurosonography and described the features of median nerve in carpal tunnel[91]. He used 5-7.5 MHz linear array transducer.

In 2000, Martinoli et al. first did a study on peripheral nerve sonography in leprosy.

With advancement in technology, Ultrasonogram imaging improved in quality through introduction of high frequency and high resolution broad band linear array transducers upto 18 MHz and newer image processing technologies.

Ultrasound imaging is a better choice than MRI for peripheral nerve imaging for many reasons[92]

1. It is an operator dependent technology
2. Dynamic examination and assessment of nerves possible
3. Bedside availability
4. Low cost.
5. Non invasive

US of peripheral nerve imaging on longitudinal scan shows characteristic fascicles appearing as alternating hypoechoic (fascicles) and hyperechoic bands (epineurium) giving the "Bundle of straw" appearance.

Cross section shows round or oval structure with hypoechoic areas (fascicles) surrounded by hyperechoic area representing connective tissue.

Deep technical skills and anatomic knowledge are essential for good scanning techniques. HRUS of nerve requires linear high frequency transducer. (>10 mHz)

Early recognition and prompt treatment with steroids and nerve release surgery can reverse the nerve damage in leprosy reaction[3]. Routinely nerve assessment in leprosy is carried out through clinical examination and nerve conduction study. HRUS of peripheral nerves is a non-invasive method which provides information on location, and degree of nerve enlargement. Alteration in nerve morphology, echogenicity, fascicular pattern and vascularity of nerve reflects the histological changes[3]. HRUS is an excellent tool for studying structural changes in nerves that cannot be biopsied[6]. Since the invasive investigations like Slit Skin Smear, Nerve Biopsy and skin biopsy place the treating physician at the risk of HIV and HBV there is a need for alternate ways for confirming the diagnosis.

Palpation of peripheral nerve is highly subjective and significant inter-observer variation exists.

Technical requirements:

High resolution linear array transducers are an essential prerequisite for HRUS. The frequency of transducers largely depends on the location of nerves. For superficial nerves, 12-18 MHz is recommended. For deeper nerves, lower frequencies are used (5-7.5 MHz). Image quality depends on spatial and contrast resolution[93].

Use of 22MHz transducer allows visualization of inner part of small cutaneous nerves[94] e.g. Sural nerve and enables measurements of nerve fascicles. This could be invaluable in assessing cutaneous nerve neuropathy.

In addition to this, high quality colour Doppler and duplex function helps in evaluation of nerve vascularity. This proved to be useful in picking up reactional states in leprosy nerve tumour and inflammatory nerve diseases.

For performing HRUS, examiner should have thorough knowledge and expertise of musculoskeletal topographic anatomy.

EXAMINATION TECHNIQUE:

Peripheral nerves can be easily identified by certain anatomical landmarks such as bones, tendons or blood vessels.

The examination of peripheral nerve usually begins with transverse section. After that nerve can be traced proximally and distally in cross sections. Then the pathological change is examined longitudinally also.

Since the peripheral nerve changes its depth during their course in extremities, meticulous adjustment of electronic focus and frequency of probe is very crucial.

In normal weight persons, all major nerves of extremities can be assessed in their full course. In obese persons, examination of sciatic nerve in thigh and tibial nerve on lower leg is difficult. In thin persons, even small sensory nerves of lower extremities e.g. sural, saphenous, supercficial peroneal nerve can be assessed[95].

ULTRASOUND ANATOMY OF NERVE:

On cross section, nerve appears round to oval and shows “honey comb appearance” due to fascicles. Fascicles are hypoechogenic surrounded by echogenic rim of interfascicular epineurium and perineural sheath. Fascicles are the smallest structure visible through HRUS. Axons

are not visible. The number of fascicles differs depending on the type of nerve, its location and its size.

NERVE ULTRASOUND:

HRUS provides real time examination of soft tissues in static and dynamic states[3]. Nerve sonography shows five main pathologic alterations:

1) Enlargement of nerves.
2) Increased hypoechogenicity or hyperechogenicity
3) Enlarged fascicles.
4) Increased thickness of epineurium[3].
5) Increased endoneural and epineural blood flow.

Sites of examination of peripheral nerves-

- ✓ Median nerve can be examined at wrist and forearm
- ✓ Ulnar nerve at elbow and proximal to medial epicondyle
- ✓ Lateral popliteal nerve at fibular head
- ✓ Posterior tibial at ankle and proximal to medial malleolus[3]

The length of abnormality of nerve can be measured by tracing above and below the course. All nerves are measured on cross sections at point of maximum nerve thickness in the visualised segment.

ENLARGEMENT OF NERVES:

The cross sectional area of the nerve is obtained from the area within the inner margin of hyperechoic rim[96, 97, 98].

ECHOGENICITY:

The echogenicity is assessed at multiple regions on transverse sections[99].

Grading of nerves based on echogenicity are

- Normal - normoechogenic
- Mild - some hypoechogenicity
- Moderate -Obvious hypoechogenicity
- Severe - absence of fascicular pattern

Size of fascicles:

Scanning of nerves along its length enables determination of fascicle size on transverse section. Enlargement has been noted in Chronic inflammatory demyelinating polyneuropathy (CIDP), Charcot Marie Tooth hereditary neuropathy and leprosy[3].

Epineurial thickness:

- ✓ It is measured on transverse plane.
- ✓ Its thickening correlates with nerve enlargement.

Vascularisation of nerve:

Colour Doppler or Power Doppler is used to assess vascularisation. Colour Doppler settings are optimised to analyse weak signals from blood vessels with slow velocity[6].

Based on sonographic appearance:

Nerves are classified as[5,6]

Group I - Normal

Group II - Enlarged with fascicular abnormalities

Group III - No fascicular pattern visible

Nerves with inflammation during reversal reaction show hypervascularity on Colour Doppler.

NERVES IN LEPROSY AND SONOGRAPHY:

HRUS provides a new dimension in diagnosis of neural involvement in leprosy, particularly pure neuritic forms[100].

In leprosy, thickened nerves are assessed by clinical palpation routinely at their superficial course. HRUS allows study of nerve not limiting to its subcutaneous course but allows in deeper plane. Even small morphologic changes and subtle anatomic variation are noted which is not clinically assessed.

Nerve biopsy is routinely done to see the changes of inflammation and is done on cutaneous sensory nerves. HRUS enables the study of nerve trunk involved directly and to look for hypervascularity. It may avoid invasive biopsy .

Even in the absence of signs and symptoms of reversal reaction, HRUS can show the early hemodynamic changes in epineurium and endoneurium. This helps in finding out the progression to reactional state early and to start corticosteroid therapy at right time .

HRUS can guide FNAC procedure of nerve by showing the exact site of pathology within the nerve to be aspirated.

Patient in reactional state can be followed up by HRUS and colour Doppler to determine the vascular flow. This help in assessing improvement and prognosis.

HRUS can detect nerve abscess along the nerve.

Recommendations for HRUS in leprosy:

1) Pure neuritic leprosy
2) Patients with symptoms of peripheral neuropathy and hypopigmented patch but no anaesthesia.
3) Silent nerve paralysis- absence of nerve tenderness but signs of peripheral neuropathy
4) In all leprosy patients to assess thickening of nerves, hemodynamic changes.

AIM OF THE STUDY

1. To study the clinical spectrum of Leprosy patients.
2. To assess the peripheral nerves clinically by palpation and then by high resolution ultrasonography and colour doppler
3. To correlate the ultrasonographic findings with clinical findings.

MATERIALS AND METHODS

3.1 Type of study : Cross sectional, Prospective, Observational study

3.2 Study approval : Prior to commencement of this study - Thesis & Ethical Committee of Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai had approved the thesis protocol.

3.3 Place of study : Rajiv Gandhi Government General Hospital

3.4 Period of study : Duration starting from October 2015 to August 2016

3.5 Sample size : Study included two groups- 30 cases and 30 controls

3.6 Selection of patients:

FOR CASES

INCLUSION CRITERIA:

- ✓ All newly diagnosed Leprosy patients with or without neuritis attending Leprosy clinic in RGGGH, Chennai.

EXCLUSION CRITERIA:

- ✓ Patients with causes of neuropathy other than Hansen's disease (Diabetes mellitus, Vasculitis, Hypothyroidism, Chronic renal failure, Vitamin B12 deficiency)
- ✓ Patients less than 18 years

FOR CONTROLS

INCLUSION CRITERIA:

- ✓ Age and sex matched healthy Individuals

EXCLUSION CRITERIA:

- ✓ Patients with causes of neuropathy other than Hansen's disease (Diabetes mellitus, Vasculitis, hypothyroidism, chronic renal failure, vitamin B12 deficiency)

3.7 Study procedure:

Around 30 newly diagnosed leprosy patients were selected from the patients attending Leprosy clinic in Department of Dermatology, Madras Medical College. All patients were explained about the nature of study. Informed written consent will be obtained from all patients before initiation of the study.

Detailed history along with demographic details such as age, sex, occupation will be obtained and patients will be evaluated as follows

1) General and systemic examination.
2) Dermatological examination.
3) Systematic and complete examination of skin for patches, thickening of nerves, sensory and motor examination related to ulnar, radial cutaneous, median, lateral popliteal and posterior tibial nerves.

- Nerves were clinically graded after palpation as follows.

Grade 0: nerve not thicker than the contralateral nerve and with normal sensation

Grade 1: affected nerve thicker than the contralateral nerve

Grade 2: thickening of the affected nerve which feels rope like

Grade 3: thickened nerve which feels beaded or nodular.

4) Investigations namely Slit skin smears for AFB ,complete hemogram, liver function tests and renal function tests.
5) Skin biopsy and nerve biopsy were done in suspected cases to confirm the diagnosis.
6) Nerve conduction studies to exclude other neurological causes were done in pure neuritic type of leprosy .
7) High resolution Ultrasonic (HRUS) imaging of the peripheral

nerves for cross-section area , texture and vascularity was done. Bilateral peripheral nerves were imaged by an independent radiologist blinded to the clinical diagnosis using ultrasound with linear array broadband frequency of 10-14 MHz.

Bilaterally, the ulnar nerve at the elbow and proximal to the medial epicondyle , the radial cutaneous nerve at wrist ,the median nerve at the wrist, Lateral Popliteal nerve at the fibular head and Posterior tibial nerve at the ankle and proximal to the medial malleolus were examined and the length of abnormality of the nerve was determined by the presence of abnormal size and echo reflectivity of the nerves.

All nerves were measured on transverse sections at a point where the nerve thickness is maximum in the visualized segment of the nerve. On transverse scans, the cross-sectional area of the nerve was determined from that area by one measurement within the hyperechoic rim surrounding the nerve.

Echo texture of the nerves assessed on imaging was graded as follows:

Normal= normoechogenic (grade 0)
Mild =some hypo-reflectivity(grade 1)
Moderate = obvious hypo-reflectivity (grade 2)
Severe= absence of any fascicular pattern. (grade 3)

Color Doppler (CD) settings were optimized to identify the weak signals from vessels with slow velocity. Band filter 50Hz, Pulse repetition frequency of 1 KHZ and Doppler gain was adjusted to the maximum level to prevent clutter. Perineural and endoneural blood flow were looked for and noted.

3.8 Follow up

Patients were advised to come for review after 1 week according to the investigations taken. The reports of all the investigations and opinion were collected and recorded.

3.9 Variables studied:

Independent variables:

- ✓ Age
- ✓ Sex
- ✓ Occupation
- ✓ Sensory and Motor deficits
- ✓ Number of patches
- ✓ Number of nerves involved clinically – Thickness ,Tenderness
- ✓ Presence of Reactions –Type 1 or Type 2
- ✓ Cross sectional area on HRUS
- ✓ Texture of the nerves
- ✓ Vascularity of nerves

3.10 Ethical consideration

All the patients were given an explanation of the study and about the investigative and operative procedures with their merits and demerits, expected results, and possible complications. Patients who agreed to participate in the study were included in the study. The study did not involve any additional investigation or any significant risk. It did not cause economic burden to the patients. The study was approved by the institutional review board prior to commencement of data collection. Informed consent was taken from each patient. Data were collected by approved data collection form.

3.11 Data collection

Using pretested proforma, patient details, clinical findings, Investigations and treatment were recorded. All the data collected were analyzed statistically.

3.12 Data analysis

Data analysis was done both manually and by using computer. Calculated data were arranged in systematic manner, presented in various table and figures and statistical analysis was made to evaluate the objectives of this study. Results obtained on the basis of high resolution sonographic study of peripheral nerves of the patients will be compared with those of healthy normal volunteers with the help of Statistical

Package for Social Science (SPSS) version 22.

- For comparison of group differences, the nonparametric test - Wilcoxon-Mann-Whitney test was used.
- For the comparison of proportions , the χ^2 test (Kruskal-wallis test) was used. Spearman test used for correlation of certain variables.
- Probability (p) values less than 0.05 were considered significant.

OBSERVATION AND RESULTS

TABLE 1 : Distribution of Leprosy patients according to Age & Sex

Age (in years)	Male	Female	Total
20-24	3 (10%)	1 (3.3%)	4 (13.3%)
25-29	4 (13.3%)	2 (6.7%)	6 (20%)
30-34	4 (13.3%)	1 (3.3%)	5 (16.6%)
35-39	1 (3.3%)	2 (6.6%)	3 (10%)
40-44	3 (10%)	2 (6.6%)	5 (16.6%)
>45	3 (10%)	4 (13.3%)	7 (23.3%)
	18	**12**	**30**

It was observed that age of 30 patients ranged from 20-46 years. Most of the patients (23.3%) were belonged to the group above 45 years. Males were 18 (60%) in number while females were 12 (40%) in number.

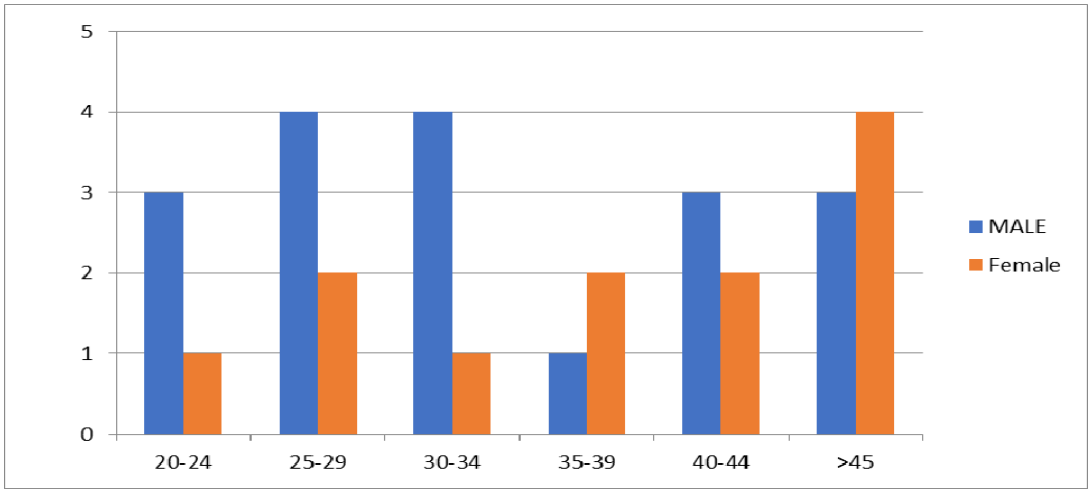

Chart 1 : Distribution of Leprosy patients according to Age & Sex

TABLE 2: Distribution of Leprosy patients according to duration of symptoms

Duration of Symptoms (in months)	No. of patients
2-6	14 (46.7%)
7-12	9 (30%)
13-18	2 (6.7%)
19-24	5 (16.6%)

In this study, the patients had duration of symptoms ranging from 2 to 24 months, with mean duration 11 months. Most patients 14 (46.7%) had symptoms for 2-6 months followed by 9 patients (30%) had symptoms for 7-12 months duration.

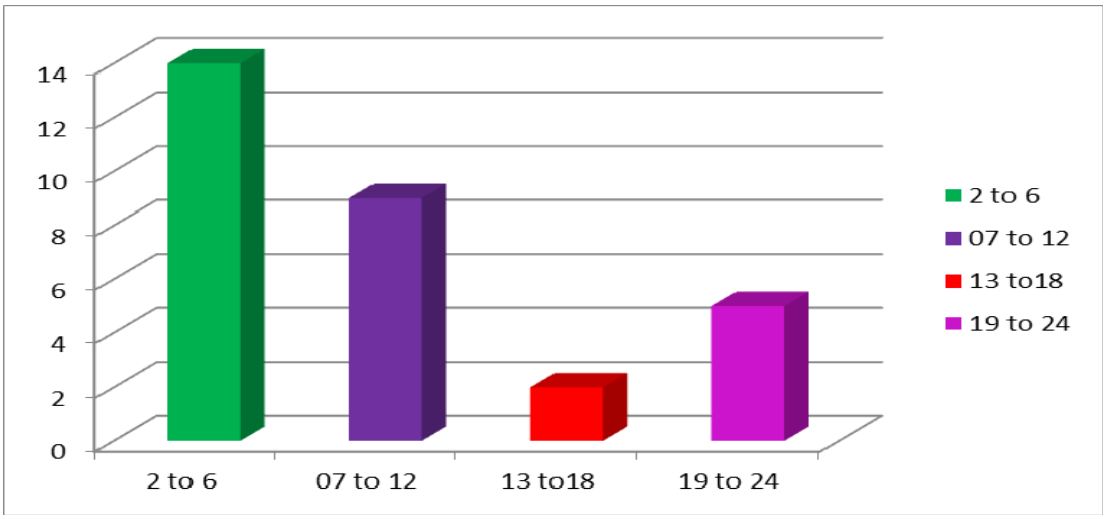

CHART 2: Distribution of Leprosy patients according to duration of symptoms

TABLE 3: Distribution of Leprosy patients according to Clinical Spectrum (Ridley-Jopling Classification)

Spectrum of Disease	No. Of Patients	% (Of Patients)
BL	6	20
BT	14	46.6
LL	5	16.7
PNL	5	16.7
Grand Total	**30**	**100**

In our study, most of the patients belonged to Borderline tuberculoid spectrum of disease 14 (46.6%) followed by Borderline lepromatous 6 patients (20%) and Lepromatous and Pure neuritic leprosy constitutes 5 patients (16.7%) each.

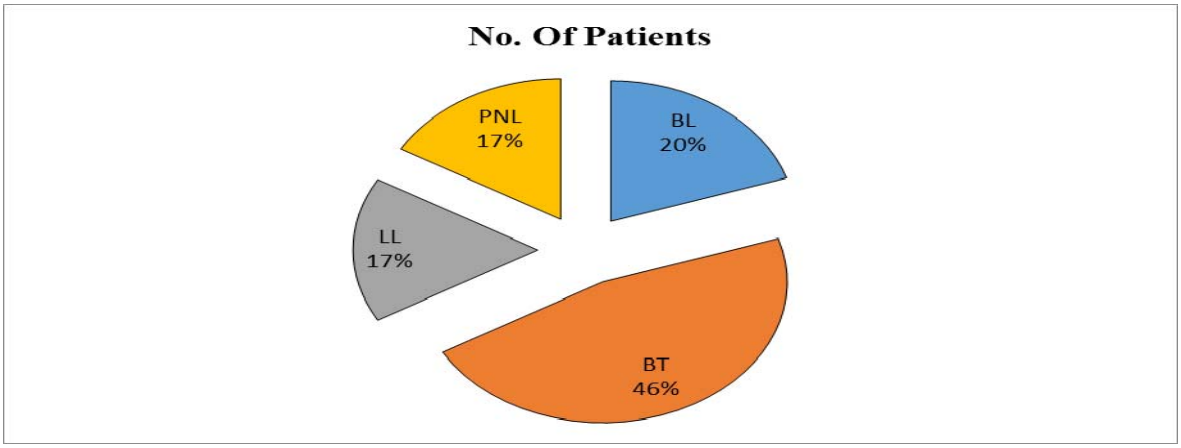

CHART 3: Distribution of Leprosy patients according to Clinical Spectrum

TABLE 4 : Reactional state among Leprosy patients

Reaction status	No. Of Patients
Without Reaction	24 (80%)
With Reaction	6 (20%)
Grand Total	**30**

Out of 30 patients included in the study, six patients (20%) were in reaction state, 4 of them were in type 1 reaction and 2 of them had type 2 reation.

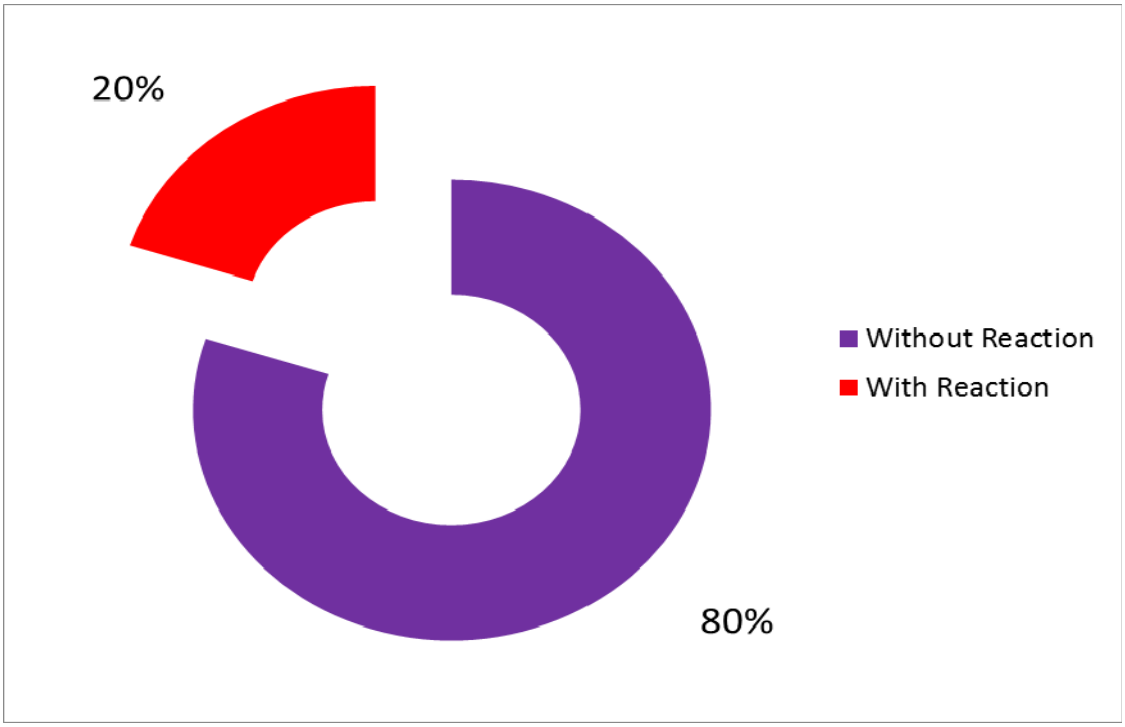

CHART 4 : Reactional state among Leprosy patients

TABLE 5 : REACTIONAL STATES IN VARIOUS CLINICAL SPECTRUM

With Reaction	No. Of Patients
BT	3
BL	2
LL	1
Total	**6**

Among six patients with reaction, 3 were in Borderline tuberculoid leprosy, 2 were in Borderline lepromatous and 1 patient in Lepromatous leprosy.

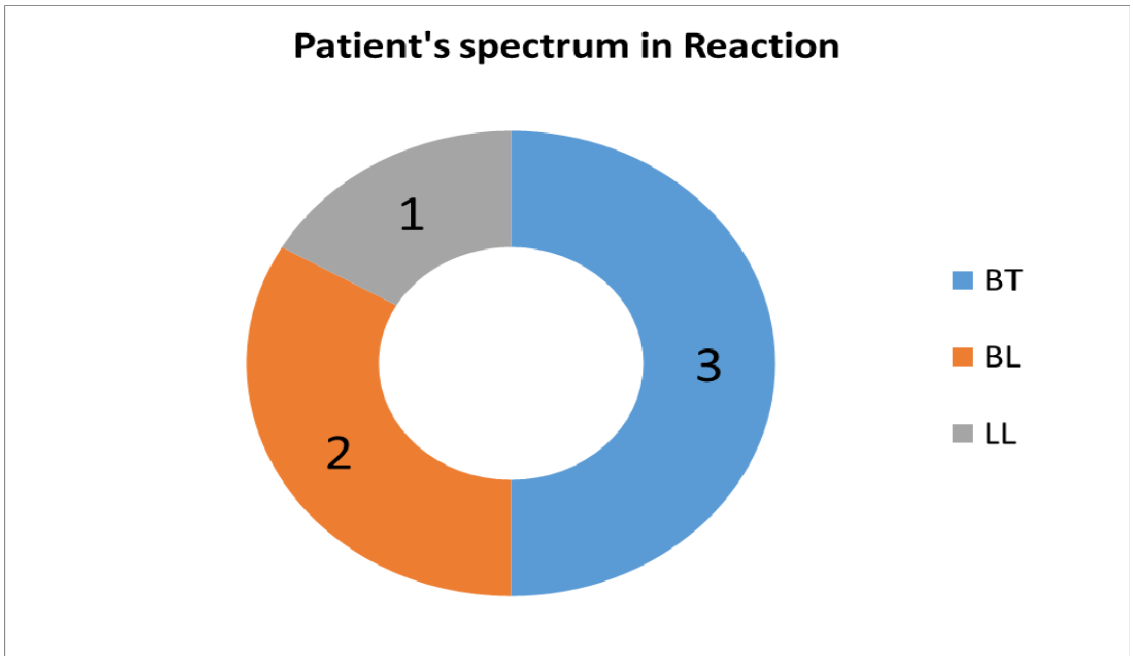

CHART 5: Number of patients in reaction with respect to spectrum

TABLE 6 : NUMBER OF PATCHES ON CLINICAL EXAMINATION

Patches Range	No. of Patients
No patch	5 (16.6%)
< 10	14 (46.7%)
> 10	11 (36.7%)
Grand Total	**30**

Among 30 patients included in the study, 14 patients had less than 10 patches and 11 of them had more than 10 patches. 5 patients (36.7%) had no skin lesions at the time of presentation.

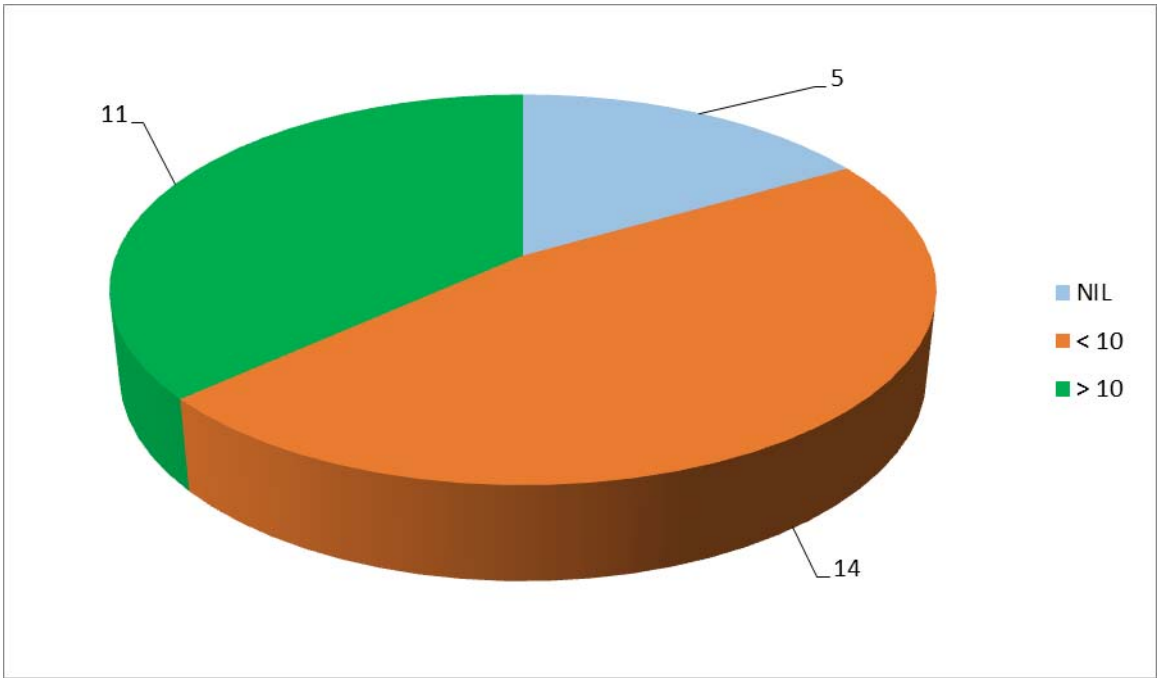

CHART 6 : NUMBER OF PATCHES ON CLINICAL EXAMINATION

TABLE 7 : NUMBER OF NERVES ON CLINICAL EXAMINATION

No.of nerves involved	No. of Patients	Percentage %
1	5	16.7
2	13	43.3
3	3	10
4	8	26.7
5	1	3.3
Grand Total	**30**	**100**

In our study among studied 30 leprosy patients , 5 patients had single nerve involvement , 13 patients had two nerves involved. In eight patients, four nerves were involved. One patient got five nerves involved.

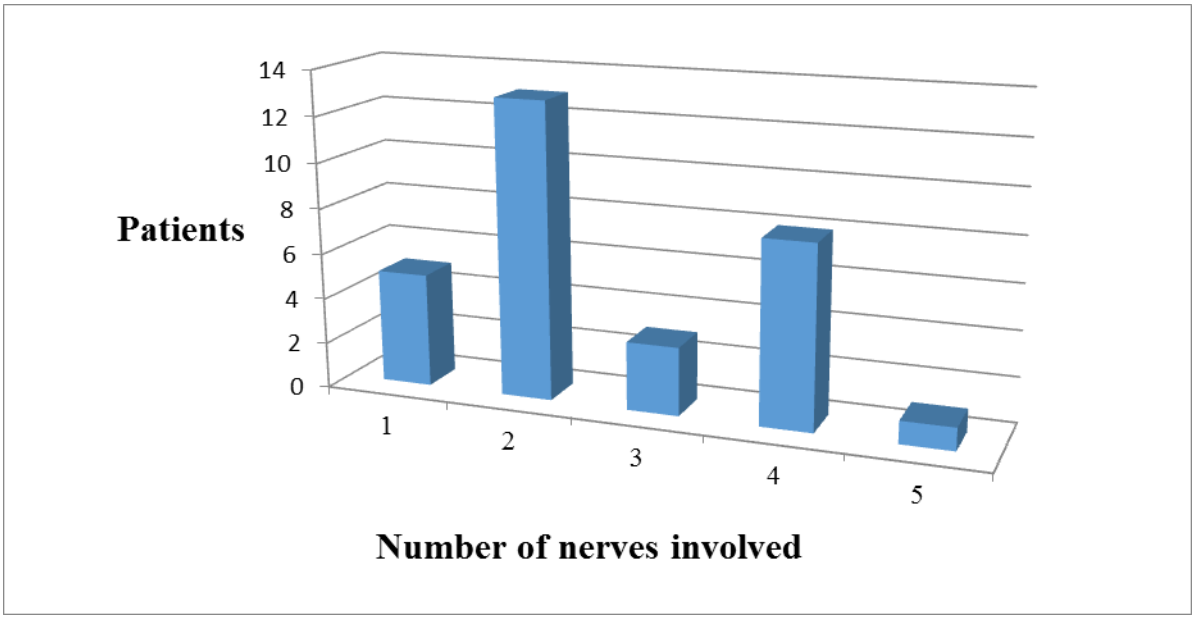

CHART 7 : NUMBER OF NERVES INVOLVED ON CLINICAL EXAMINATION

TABLE 8 : MOTOR OR SENSORY DEFICIT IN LEPROSY PATIENTS

Motor and Sensory Deficits	No. Of Patients
Motor Deficiency with Sensory Deficits	3 (10%)
Motor Deficiency with no sensory Deficits	2 (6.7%)
Sensory Deficiency With No motor deficits	18 (60%)
No Motor and Sensory Deficits	7 (23.3%)
Grand Total	30

On clinical examination of 30 patients included in this study, 18 patients (60%) presented with only sensory deficits such as hypoesthesia , paraesthesia. Three of them had both motor and sensory deficits. Two patient had only motor deficits. Seven patients didn't have any sensorimotor deficits.

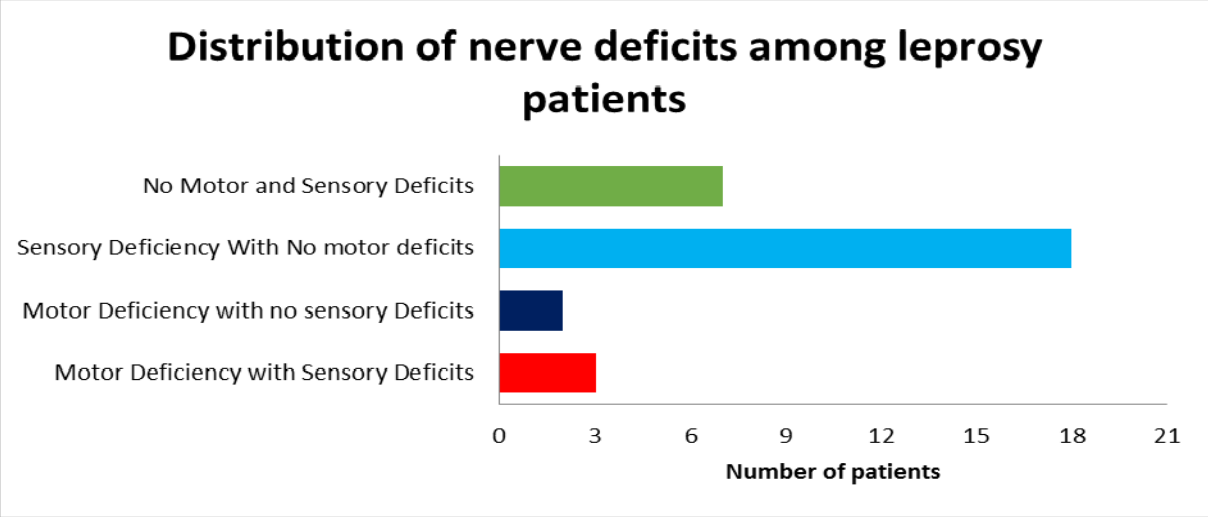

Chart 8: Distribution of neurological deficits among leprosy patients

TABLE 9 : CLINICAL GRADING OF NERVE THICKNESS

Nerves		Clinical grading of nerve thickness			
		0 Normal	1 Mild	2 Moderate	3 Severe
Ulnar Nerve (n=60)	Right	6	8	15	1
	Left	17	2	10	1
Radial Nerve (n=60)	Right	26	4	0	0
	Left	26	4	0	0
Lateral Popliteal Nerve (n=60)	Right	19	3	8	0
	Left	17	9	4	0
Posterior Tibial Nerve (n=60)	Right	25	3	2	0
	Left	26	3	1	0
Total = 240		162	**36**	**40**	**2**

In this study among 30 patients , 300 nerves (60 ulnar, radial cutaneous , lateral popliteal and posterior tibial nerve) were examined clinically. Clinical examination of nerves showed thickening of 78 nerves out of 240 nerves. (Median nerve not clinically graded) . Grade 1 thickening seen in 36 nerves , grade 2 thickening in 40 nerves and grade 3 thickness seen in two nerves. Ulnar nerve (47.5%) was most frequently

involved followed by lateral popliteal(30.7%) , posterior tibial nerve(11.5%) and radial cutaneous nerve(10.3%).

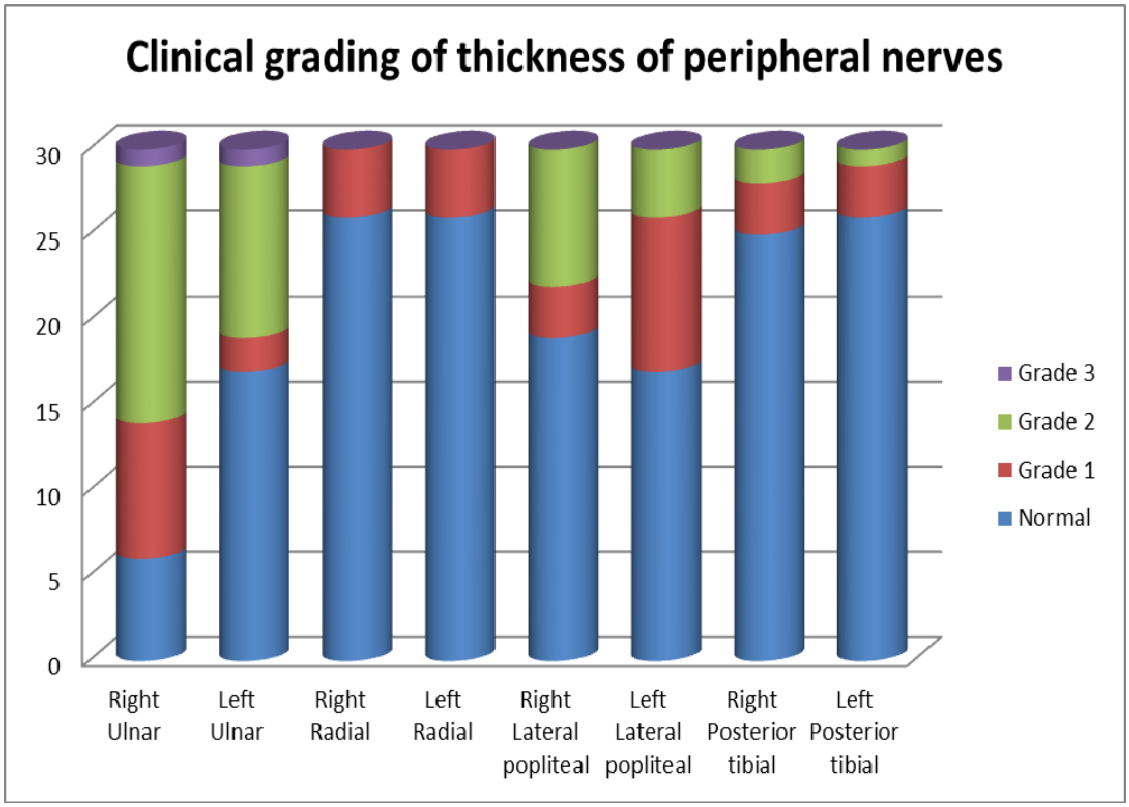

CHART 9: Distribution of nerves according to clinical grades of thickness

TABLE 10 : CLINICAL GRADING OF NERVE TENDERNESS

Nerves		Clinical grading of nerve tenderness			
		0	1	2	3
Ulnar Nerve (n=60)	Right	26	2	2	0
	Left	28	2	0	0
Radial Nerve (n=60)	Right	28	2	0	0
	Left	30	0	0	0
Median Nerve (n=60)	Right	30	0	0	0
	Left	29	1	0	0
Lateral Popliteal Nerve (n=60)	Right	28	2	0	0
	Left	28	2	0	0
Posterior Tibial Nerve (n=60)	Right	30	0	0	0
	Left	30	0	0	0
Total = 300		287	11	2	0

Among the 30 patients studied , 6 patients has tenderness on nerve palpation . 13 nerves out of 300 nerves palpated were tender.

TABLE 11 : USG GRADING OF ECHOGENICITY OF NERVE

Nerves		USG grading of echogenicity of nerve			
		0	1	2	3
Ulnar Nerve (n=60)	Right	11	8	11	0
	Left	8	14	7	1
Radial Nerve (n=60)	Right	26	4	0	0
	Left	23	7	0	0
Median Nerve (n=60)	Right	18	12	0	0
	Left	21	9	0	0
Lateral Popliteal Nerve (n=60)	Right	16	9	5	0
	Left	14	15	1	0
Posterior Tibial Nerve (n=60)	Right	20	10	0	0
	Left	21	9	0	0
Total		178	97	24	1

On sonographic examination of 300 nerves, 122 nerves (40.6%) were found to be hypoechogenic and 178 nerves were normoechogenic. Among hypoechogenic nerves, 97 nerves (32.3%) showed mild hypoechogenicity, 24 nerves (8%) showed obvious hypoechogenicity and 1 nerve showed complete loss of fascicular pattern.

Table 12 : Cross sectional area of peripheral Nerves in healthy controls and leprosy patients

Subjects	Ulnar (n=60)		Radial Cutaneous (n=60)		Median (n=60)		Lateral Popliteal (n=60)		Post. Tibial Nerve (n=60)	
Controls	R	L	R	L	R	L	R	L	R	L
Mean	7.2±1.3	7.2±1.06	7.4±1.8	7.2±1.5	5.3±1.1	5.25±0.9	7.4±1.1	7.1±1.1	6.3±0.8	6.4±0.35
Median	7.4	7.4	7	6.7	5.4	5.25	7.5	7.25	6.3	6.3
Range	4.5-9.8	4.7-9.8	4.5-14.2	5.5-12.2	3.5-7.6	3.7-7.4	5.5-9.4	5.5-9.2	4.0-7.8	4.9-7.8
Leprosy Cases										
Mean	11.8±2.9	11.2±3.4	8.3±2.0	8.0±2.0	5.4±1.6	5.8±2.5	8.9±3.6	8.6±3.0	7.6±2.4	7.8±2.3
Median	12.4	10.4	8.2	8.1	5.3	5.2	7	8	6.9	6.5
RANGE	5.4-16.8	5.2-18.4	4.4-12.2	4.2-13.2	3.2-12.2	3-13.6	5.2-16.2	4.8-16	4.8-13.4	4.6-15.6
Significance										
Mann-Whitney U	90	106.5	298.5	319	449.5	439.5	408.5	350.5	332.5	393
p Value	**<0.005**	**<0.005**	**<0.025**	<0.0536	<0.99	<0.877	<0.53	<0.14	<0.08	<0.399

This table shows the mean CSA of peripheral nerves measured for both controls and cases through High resolution ultrasonography. The Mean CSA of ulnar nerve is highest in leprosy patients which is followed by lateral popliteal nerve.It was found that the mean CSA of all peripheral nerves were enlarged in patients when compared to controls.

Table 13 : Distribution of ulnar nerves based on Cross sectional area

CSA of ulnar nerves (mm2)		RIGHT	LEFT	Total
<7.2	< Mean	1	3	4
7.2-8.5	Mean+1 SD	4	4	8
8.6-9.8	Mean+2 SD	2	5	7
9.9-11.2	Mean+3 SD	**4**	**6**	**10**
>11.3	Mean+4 SD	**19**	**12**	**31**
TOTAL				**60**

Out of 60 ulnar nerves examined in leprosy patients , 31 ulnar nerves have CSA above 11.3 mm^2 (Above Mean + 4 S.D).

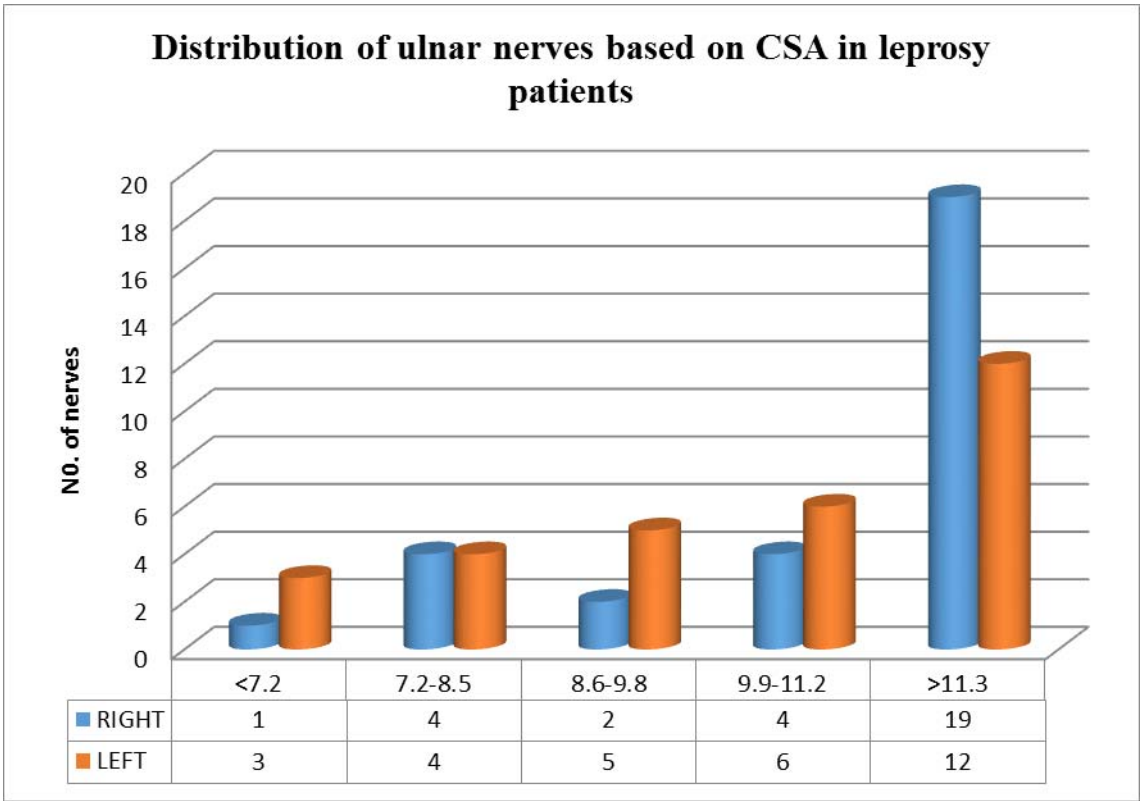

Chart 11: Distribution of ulnar nerves with increasing CSA in leprosy patients

Table 14 : Statistical significance of the relationship of clinical parameters versus ultrasonographic features of peripheral nerves in leprosy patients

Correlation of sonographically measured CSA of nerves with clinical grading of nerve thickness

Clinical Grading Of Nerve Thickness	Statistical parameters	CROSS SECTIONAL AREA							
		Ulnar		Radial Cutaneous		Lateral Popliteal		Posterior Tibial	
		Right	Left	Right	Left	Right	Left	Right	Left
	Chi-Square	20.880	19.145	10.091	1.806	10.606	16.435	10.606	6.326
	p value*	**<0.005**	**<0.005**	**<0.001**	.179	**<0.005**	**<0.005**	**<0.005**	**<0.042**

*p value significant at <0.05 level using Kruskal-Wallis test

The above tables show there is a significant correlation between clinical thickness of nerve and cross sectional area of peripheral nerves.

Table 15:

Correlation of clinical thickness of nerve with echo texture observed on ultrasonography using Spearman's rho

Clinical Grading Of Nerve Thickness	Statistical parameters	ECHOTEXTURE							
		Ulnar		Radial Cutaneous		Lateral Popliteal		Posterior Tibial	
		Right	Left	Right	Left	Right	Left	Right	Left
	Correlation coefficient	.525	.612	.712	.247	.637	- .024	.246	.598
	p value*	**<0.003**	**<0.001**	**<0.001**	<0.188	**<0.001**	<0.900	<0.191	**<0.001**

*p value significant at <0.05 level. Spearman's rank correlation

The above table show there is a significant correlation between clinical thickness of nerve and echotexture of nerve observed on HRUS.

Table 16 : Colour Doppler flow observed among leprosy patients

NERVES	FLOW PRESENT IN
ULNAR	9
RADIAL CUTANEOUS	1
MEDIAN	0
LATERAL POPLITEAL	2
POSTERIOR TIBIAL	1
TOTAL	13

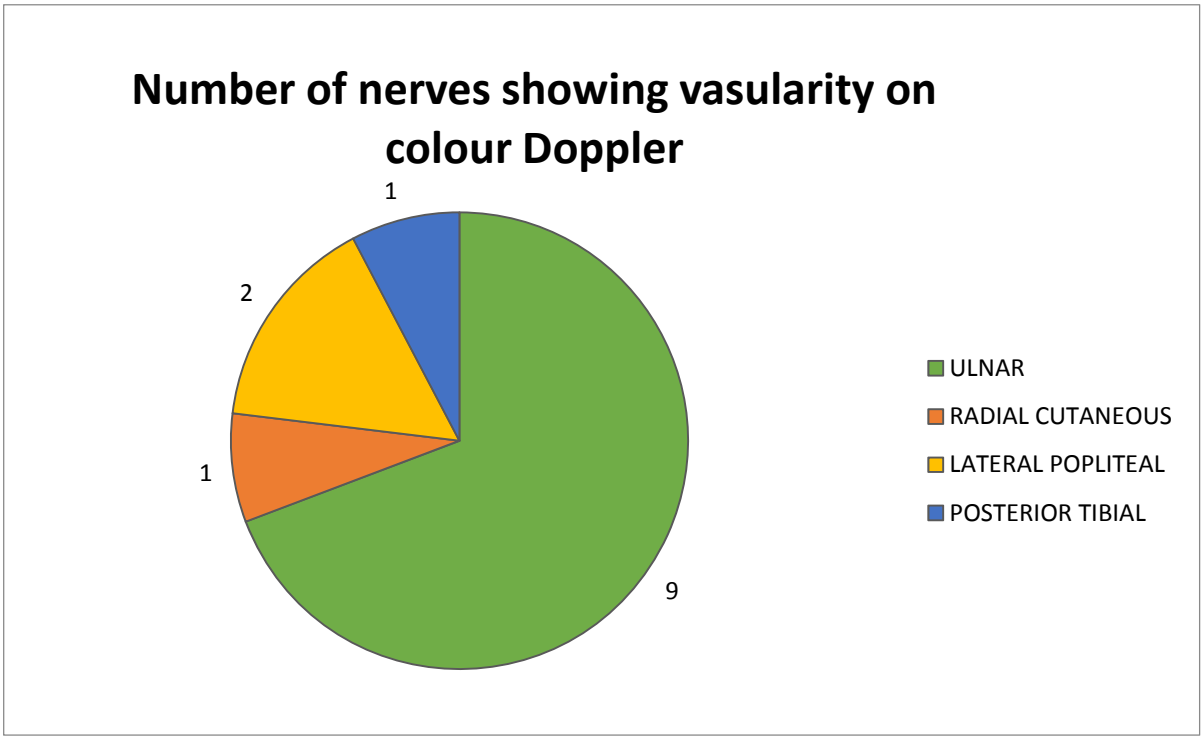

Chart 12: Flow Observed on Color Doppler of the nerves

Out of all nerves examined , 13 nerves showed blood flow in colour Doppler. Of which 9 were ulnar nerves, 2 were Lateral popliteal nerve, 1 radial cutaneous and posterior tibial nerve. Seven patients showed blood flow on colour Doppler among 30 studied patients. Six of them were in reactional state. One patient was not in reaction but showed increased flow. Four patients had flow in multiple nerves , even in clinically uninvolved nerves.

Table 17 : Clinical and HRUS findings of peripheral nerves in leprosy patients

Characteristics	Ulnar (n=60)	Radial Cutaneous (n=60)	Median (n=60)	Lateral Popliteal (n=60)	Posterior Tibial (n=60)	All Nerves (n=300)
CLINICAL FINDINGS						
THICKNESS						
Grade 0	23(38.3%)	52(86.7%)	-	36(60%)	51(85%)	162(67.5%)
Grade 1	10(16.7%)	8(1.3%)	-	12(40%)	6(10%)	36(15%)
Grade 2	25(41.7%)	0	-	12(40%)	3(5%)	40(16.7%)
Grade 3	2(3.3%)	0	-	0	0	2(0.8%)
SONOGRAPHIC FINDINGS						
1)Echotexture						
Normal	19	49	39	30	41	178(59.3%)
Mild	22	11	21	24	19	97(32.4%)
Moderate	18	0	0	6	0	24(8%)
Severe	1	0	0	0	0	1(0.3%)
2) CSA Enlargement*	42(70%)	19(31.6%)	6(10%)	12(20%)	12(20%)	91(30%)
3) Vascularity on CD	9	1	0	2	3	15(5%)

* CSA Enlargement based on values more than Mean + 2 standard deviation in controls

TABLE 18 : SONOGRAPHIC FINDINGS OF HEALTHY CONTROLS

Controls (30)	Ulnar (60)	Radial Cutaneous (60)	Median (60)	Lateral Popliteal (60)	Posterior Tibial (60)	Total Nerves (n=300)
ECHOTEXTURE OF NERVES						
Normoechoic	60	60	60	60	60	300
Hypoechoic	0	0	0	0	0	0
COLOUR DOPPLER FLOW						
PRESENT	0	0	0	0	0	0
ABSENT	60	60	60	60	60	300

Among 30 controls examined through HRUS, all the 300 nerves examined showed normoechogenicity and there was no vascular flow detected in the peripheral nerves on colour Doppler. All the 300 nerves showed absent blood flow.

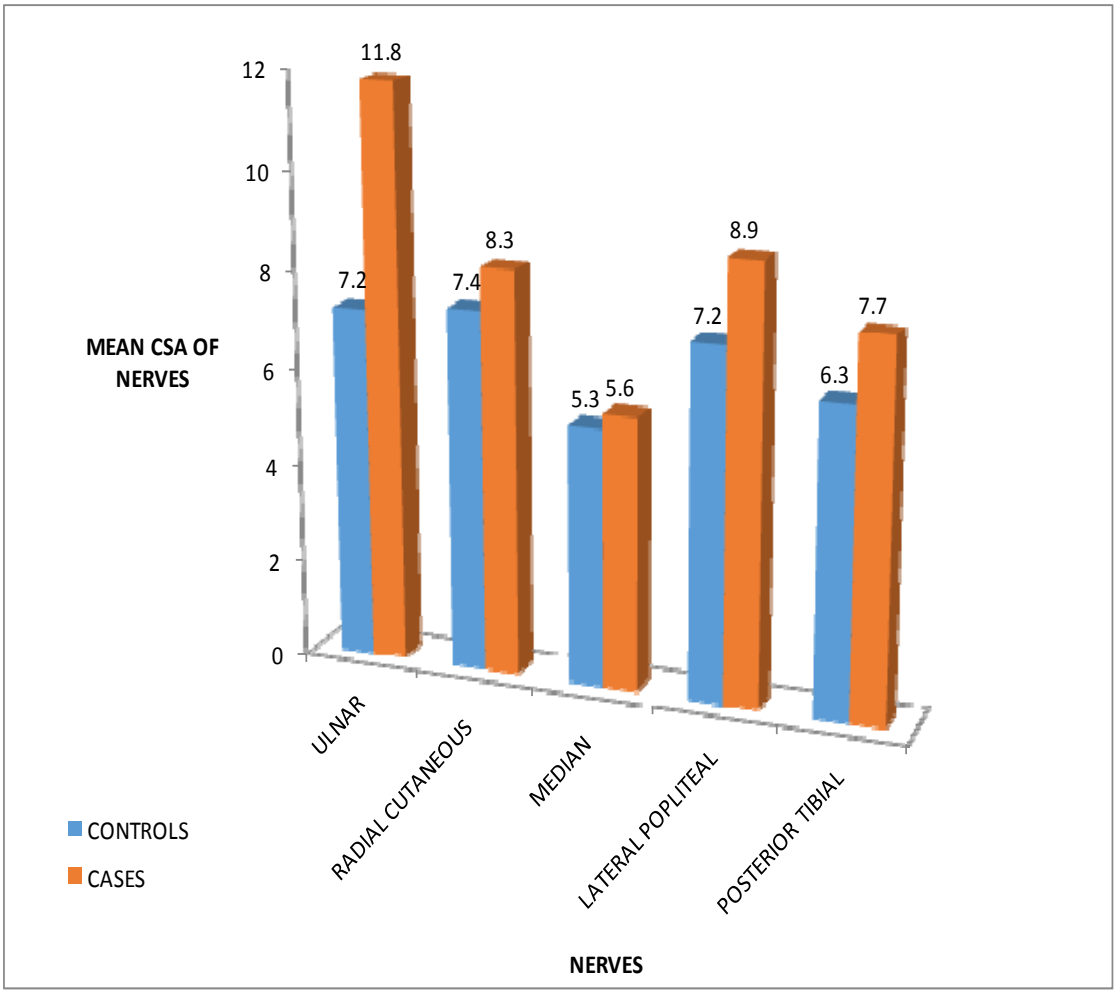

CHART 13 : COMPARISON OF CROSS SECTIONAL AREA OF NERVES OF CASES AND CONTROLS

Figure 1: High resolution ultrasound of normal ulnar nerve at elbow. (Yellow circle)

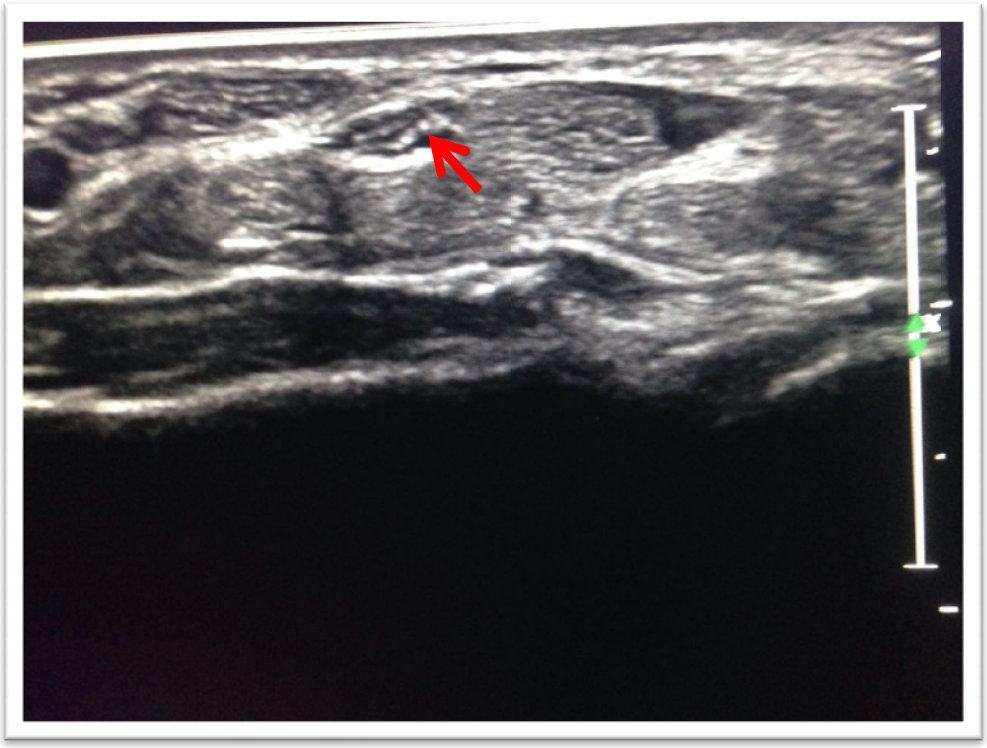

Figure 2: Normal median nerve at wrist on ultrasound (Red arrow)

Figure 3: Loss of fascicular pattern seen on ulnar nerve of patient with leprosy (Dotted ellipse)

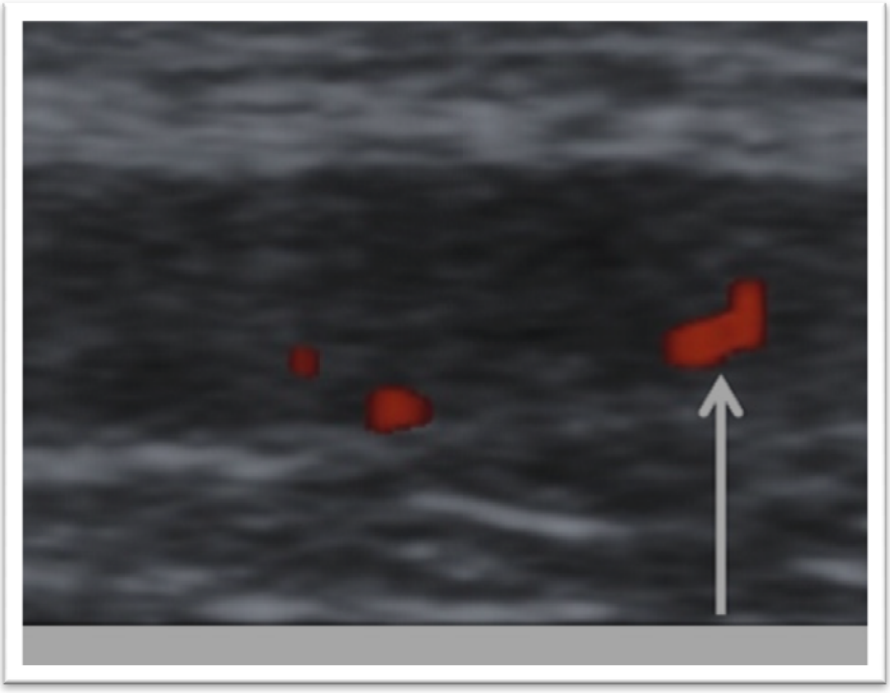

Figure 4: Colour Doppler showing vascularity in ulnar nerve in a patient with type 1 reaction

DISCUSSION

This prospective, observational study was conducted among the patients attending leprosy clinic in Department of Dermatology, Venereology and Leprosy at RGGGH, Chennai. This study was carried out with the view of assessment of peripheral nerves with HRUS and Colour Doppler and to determine its usefulness in diagnosis and monitoring of leprosy patients.

Clinical examination of peripheral nerves is very subjective and has interobserver variation. In order to determine the thickness of nerve precisely ultrasonography has been used. HRUS paves way for new dimension in evaluating the morphological characteristics of nerve which is routinely assessed through invasive biopsy.

Thirty newly diagnosed leprosy patients were selected from leprosy clinic before initiation of treatment. Other causes of peripheral neuropathy were ruled out. Age and sex matched thirty healthy controls were taken from the community and other causes of peripheral neuropathy were ruled out. Controls were selected in the study to obtain reference values for cross sectional area of peripheral nerves and were subjected to HRUS examination . Informed written consent was obtained from both cases and control.

DEMOGRAPHIC DATA:

In our study, 30 healthy controls and 30 leprosy patients were selected. Both were age and sex matched.

In **Jain et al.**[6] study, 30 healthy controls and 20 leprosy patients were studied.

In another study by **Martinoli et al.**[101], 23 patients were studied for nerve abnormalities using ultrasonography , Doppler and MRI.

In a study by **Elias et al.**[102], 21 patients and 20 controls were studied.

In **Bathala et al.**[103] study included 21 patients and 22 controls.

In **Visser et al.**[104] study included 26 patients and 25 controls.

STUDY (YEAR)	Leprosy Patients (n)	Controls (n)
Martinoli et al.[101] (2000)	23	20
Jain et al.[6] (2009)	20	30
Elias et al.[102] (2009)	21	20
Bathala et al.[103] (2012)	21	22
Visser et al.[104] (2012)	26	25

In our study, age of the study population ranged from 20 to 46 years with mean age of 34.9 years. Most patients 7 (23.3%) belonged to the age group of 45-46 years followed by 6 patients (20%) belonged to age group of 20-25 years.

In **Jain et al.**[6] study, age group ranged from 12 to 52 years for patients and 17 to 58 years for controls with mean age of 33±10 years.

In **Elias et al.** study, 21 patients age ranged from 10 to 71 years with mean age of 47.7 ± 17.2 years and 20 control participant's mean age was 46.5 ± 16.2 years[102].

In **Bathala et. al.** study, mean age of the patients was 30 ±12.97 years and the range was 13–61 years. For controls, mean age was 34.6± 15 years and range was 18–70 years.

In our study, males were 18 in number and constitute 60% of the study population whereas females were 12 in number (40%) in the ratio of 3:2.

In other studies , sex distribution were as follows

STUDY (YEAR)	Leprosy Patients (n)		Controls (n)	
	Male	**Female**	**Male**	**Female**
Jain et al. (2009)	18	2	15	15
Elias et al. (2009)	12	9	14	6
Bathala et al. (2012)	19	2	20	2
Visser et al. (2012)	23	3	15	10
Our study	18	12	18	12

Out of 30 patients studied, mean duration of symptoms was 11.03 months with standard deviation 8.0 months. The duration of symptoms ranged from 2 months to 24 months. Most of the patients (14 patients-46.7%) had symptoms for 2-6 months . 7 patients (23.3%) had symptoms for more than a year. None of them had taken treatment during this period.

In **Jain et al.** study , duration of symptoms ranged from 3 to 180 months with mean of 24.7± 39.8 months[6].

CLINICAL CHARACTERISTICS:

In our study of 30 patients, 14 patients (46.7%) had skin lesions less than 10 in number whereas 11 (36.7%) patients had more than 10 skin lesions. Only five (16.6%) patients did not have any skin lesions.

In our study, all the patients had nerve involvement. Five patients (16.6%) had single nerve involvement clinically. Rest of them had more than one nerve involved. Majority of the patients (13 patients-43.3%) had two nerves involved. In eight patients (26.7%), four nerves were involved. Five nerves were involved in one patient. Most commonly involved nerve in our study was ulnar nerve followed by lateral popliteal nerve.

In **Jain et. al.** study, 18 patients had one or more nerve involvement and 2 patients had no nerve involvement.

In our study, on clinical examination of 30 patients, 18 patients (60%) presented with only sensory deficits . Three patients had both motor and sensory deficits. Two patients presented only with motor deficits. Seven patients didn't have any sensorimotor abnormalities.

In **Jain et al**. study, 12 patients showed sensory loss,15 patients showed motor weakness and 9 patients showed both sensory and motor weakness

In **Bathala et al.**[103] study of ulnar neuropathy in Hansen Disease, 32 ulnar nerves (76%) showed motor deficits , 18 nerves (43%) showed sensory loss, 18 nerves showed both motor weakness and sensory loss and 10 nerves did not showed any sensorimotor abnormalities.

Out of 30 patients in our study, 14 patients (46.6%) had Borderline tuberculoid leprosy , 6 had Borderline lepromatous (20%) , 5 had Lepromatous leprosy (16.7%) and 5 had Pure neuritic leprosy (16.7%) .

Whereas in **Jain et al.**[6] study, ten patients had borderline tuberculoid, 3 borderline lepromatous and 7 lepromatous leprosy.

In **Bathala et al.**[103] study, six patients (29%) belonged to borderline tuberculoid leprosy , 4 (19%) in borderline lepromatous, 9 (42%) in lepromatous leprosy, and 2 (10%) were in pure neuritic type of leprosy.

In **Visser et. al.**[104] study , out of 26 leprosy patients, 7 (27%) had borderline tuberculoid leprosy, 6 (23%) had borderline lepromatous

leprosy, 10 (38.5%) had lepromatous leprosy and 3 (11.5%) had pure neural leprosy (PNL).

Whereas in **Elias et al.**[102] study, five out of 21 patients had polar tuberculoid form, 7 had borderline tuberculoid form, 4 had polar lepromatous form , 2 had borderline lepromatous form and 3 had midborderline form of leprosy.

In our study, six patients (20%) were in reactional state, 4 patient had type 1 reaction and 2 patient had type 2 reaction with neuritis. Remaining 24 patients didn't show any evidence of reaction.

Whereas in other studies , reactions were seen in patients as follows:

In Martinoli et al. study, 14 nerves out of 58 nerves studied were in reversal reaction whereas in Jain et. al 16 patients showed reactions.

STUDY (YEAR)	Reaction status
Martinoli et al. (2000)	14 nerves
Jain et al. (2009)	16 patients (12 in Type 1 ,4 Type 2)
Our study	6 patients (4 in type 1, 2 in type 2)

Clinical thickening of peripheral nerves were assessed and graded from grade 0 to 3. Table 9 shows the grading of thickness of peripheral nerves.

Out of 240 nerves examined,

- 37 ulnar nerves were thickened.
- 24 lateral popliteal nerves were thickened.
- 9 posterior tibial nerves were thickened.
- 8 radial cutaneous nerves were thickened..

78 (32.5%) nerves were thickened (grade 1 to 3).

Whereas in a similar type of study by **Jain et. al.**, out of 120 nerves,

- 33 ulnar nerves were thickened.
- 30 lateral popliteal nerves were thickened.
- 23 posterior tibial nerves were thickened.

In Jain et al. study, out of 120 nerves , 86 nerves (71.6%) were thickened clinically whereas in our study , 78 nerves out of 240 (32.5%) were thickened . This could be due to higher sample size in our study and variation in clinical spectrum of patients and reactional state.

In our study, thirteen nerves out of 300 nerves examined were tender. Six patients had tender nerve on palpation and were in reaction whereas **Jain et al** observed tender nerves in 14 patients with reaction.

Sonographic characteristics:

Normal nerve appeared on HRUS examination as round or oval shape with internal hypoechogenic dots representing fascicles on transverse section. Perineurium and epineurium were hyperechoic and no blood flow signals are noted on Colour Doppler. The mean CSA were obtained for all peripheral nerves such as ulnar, radial cutaneous, median, lateral popliteal and posterior tibial nerve in both controls and cases and were tabulated in Table 12

In our study, the mean CSA of ulnar nerve for controls was found to be 7.2 mm^2 with standard deviation of 1.3 mm^2 and for cases, it was 11.8 ± 3.1 mm^2 . The mean CSA of different nerves of controls versus leprosy patients were tabulated in table 12 .

In a similar study by **Jain et al.**, mean CSA observed for ulnar , median , lateral popliteal and posterior tibial nerve were as follows:

	Mean CSA (in mm^2)			
	Controls		**Cases**	
Nerves	**Jain et al**	**Our study**	**Jain et al**	**Our study**
Ulnar	8.56± 3.5	7.2±1.1	22.7 ± 19.4	11.8 ±3.1
Median	6.26± 2.2	5.3±1	14.7± 11.6	5.6 ±2.8
Lateral popliteal	5.96± 3.2	7.2±1.1	12.8± 7	8.9 ±3.3
Posterior tibial	6.36± 3.2	6.3±0.5	12± 8	7.7 ±3.5

The mean CSA of controls observed in our study group is almost comparable with that of **Jain et al** study. The mean CSA of cases were significantly higher than that of controls in both the studies. The higher mean CSA of cases observed by **Jain et al** could be due to inclusion of more number of patients in reactional state and longer duration of disease whereas in our study, patients in reaction were less in number.

Whereas **Bathala et al.**[103] observed , the mean CSA of ulnar nerve above the medial epicondyle was 18.6± 15 mm^2 as compared with controls 4.86±1.12 mm^2 ($p < 0.0001$).

In **Elias et. al.**[102], the mean CSA of ulnar nerve was 7.05 ± 1.66 mm2 in the control group and 16.18 ±13.84 mm2 in the leprosy group ($p<0.05$). Similar to the above studies, the mean CSA of ulnar nerve for cases were statistically significant than controls.

In our study, the peripheral nerves were significantly thicker in leprosy patients when compared to the controls for ulnar nerve ($p< 0.005$) and for right radial cutaneous nerve ($p < 0.025$). The mean CSA of median, lateral popliteal and posterior tibial nerve of leprosy patients were higher than that of controls. Though the CSA of median, lateral popliteal and posterior tibial nerves of cases versus controls are not statistically significant, they were clinically significant.

This statistical insignificance could be due to non-involvement of those nerves in these leprosy patients or less frequent involvement. Sometimes there has been difficulty in measuring the exact CSA of lower limb nerves in obese individuals or with fat deposition around limbs. The CSA of nerve might change with height and body weight.

In our study, clinically 37 ulnar nerves and 9 posterior tibial nerves showed thickening. On HRUS, 42 ulnar nerves and 12 posterior tibial nerve showed the CSA value above the normal limit .Eight nerves (5 ulnar, 3 posterior tibial nerve) for which no thickening were observed clinically but showed significant sonographic enlargement whereas in **Jain et al.**[6] study, clinical thickening was not observed for 34 nerves (7 ulnar , 10 lateral popliteal and 17 posterior tibial nerve) but sonographic examination found 5 nerves (3 lateral popliteal and 2 posterior tibial nerve) were enlarged.

On contrary, 12 out of 24 lateral popliteal nerves that showed clinical thickening did not have sonographic enlargement.

In Elias et al study , ulnar nerves showed focal thickening in 90.5% cases.

In our study, on sonographic examination of 300 nerves, 178 nerves (59.3%) nerves were normoechoic and 122 (40.6%) nerves were

hypoechogenic. 97(32.4%) nerves showed mild hypoechogenicity, 24 (8%) of them showed obvious hypoechogenicity and 1 (0.3%) nerve showed loss of fascicular pattern whereas **Jain et al.**[6] observed 76 nerves (50%) were normoechoic and 76 (50%) were hypoechoic . Out of which 25(16.4%) nerves were mild hypoechoic, 45 (29.7%) were moderately hypoechoic and 6 (3.9%) showed fascicular pattern loss.

Among all nerves examined in our study, ulnar nerve showed more echo textural abnormality. It showed mild hypoechogenicity in 22 nerves , obvious hypechogenicity in 18 nerves and severe fascicular pattern loss seen in one nerve which was similar to Jain et al observation.

Whereas **Elias et al.**, observed hypoechoic areas (81%), loss of the fascicular pattern (33.3%), and focal hyperechoic areas (4.7%) among 42 ulnar nerves.

In our study, Colour Doppler signals were observed in 13 nerves which included 9 ulnar nerves, 2 Lateral popliteal nerve, 1 radial cutaneous and 1 posterior tibial nerve whereas in **Jain et al.** study, 39 nerves showed flow which includes 23 ulnar, 10 median , 4 lateral popliteal and 2 posterior tibial nerves.

In our study, four patients showed flow in multiple nerves. In Jain et al, 9 patients out of 16 in reaction showed increased flow in multiple nerves.

In our study, seven patients showed blood flow on colour Doppler among 30 studied patients. Six of them were in reactional state. One patient was not in reaction but showed increased flow on CD and thereby helping in early detection of impending reaction.

In our study, perineural and endoneural flow were seen more in the upper limb nerves , most commonly in ulnar nerve which was similar to Jain et al. study.

Increased blood flow is correlated with inflammation of the nerve. Patients who were in reaction showed increased flow. Similarly, increased flow was also observed in patients at risk of reactions or impending / early reaction which could aid in starting early treatment and thereby preventing nerve damage.

Significant correlation was observed between clinical grading of thickness of nerve and sonographic measurements such as CSA and echo reflectivity.

Table 14 and table 15 show the statistical significance of clinical and HRUS measured parameters.

p value for correlation of clinical thickness and the CSA of ulnar, median , lateral popliteal and posterior tibial nerve using Kruskal Wallis test was $p < 0.005$ and for radial cutaneous nerve , it was $p < 0.001$.

Correlation is statistically significant which is similar to that of **Jain et al.** study. ($p < 0.0001$)

p value for correlation of clinical thickness and the echotexture of ulnar , radial cutaneous , median , lateral popliteal and posterior tibial nerve using Spearman's rank correlation ($p < 0.05$) are tabulated in table 15 .

Correlation is statistically significant which was similar to that of **Jain et al.** ($p < 0.0001$).

In our study, there was an excellent correlation for ulnar nerve , right radial cutaneous ,right lateral popliteal and left posterior tibial nerve.

In our study, usefulness of ultrasound as an essential component in detecting nerve damage has been stated. It helps in clinical and therapeutic management of reactions. Nerve enlargement was more in patients with type 1 and 2 reactions and showed increased vascularity. Ulnar nerve was most frequently involved and showed more changes of the disease.

To conclude there was a statistically significant correlation between clinical findings of nerve assessed and sonographic measurement such as CSA, echotexture of the nerve and vascularity on Colour Doppler.

LIMITATIONS OF THE STUDY:

As this study has been carried out over a limited period of time with a limited number of patients it was not large enough to be of reasonable precision.

All the facts and figures mentioned here may considerably vary from those of large series covering wide range of time, but still then, as the cases of this study were collected from a tertiary level hospital in our country, this study has some credentials in reflecting the facts that high resolution ultrasonography was better than clinical palpation of nerves.

Another limitation of our study is that it was a cross-sectional one and only single ultrasonographic evaluation was performed .

STRENGTH OF STUDY:

Age and sex matched controls were taken to limit the differences in cross sectional area of nerves.

It was one of the few studies assessing the usefulness of HRUS in assessing the peripheral nerves.

In our study, radial cutaneous nerve had been studied which was not studied in any of the previous studies. There were only 5 studies using HRUS for evaluation of nerves.

Martinoli et al., studied the examination of the median, ulnar and posterior tibial nerves in 23 leprosy patients (58 nerves), with sonography and MRI[103].

Jain et al. (2009) compared HRUS with clinical examination for assessing nerve thickening and concluded that clinical examination of enlarged nerves in leprosy patients is subjective and inaccurate [103].In their study , most of the patients were in reactional state. They had higher mean CSA for peripheral nerves compared to our study.

SUMMARY

Leprosy is a curable disease. Clinical diagnosis is definitive but good point of care test is not available. Early diagnosis is essential in leprosy as the delay in diagnosis further worsens the nerve damage and leads to deformity and disability. HRUS is a novel technique of nerve assessment.

In our study, we have substantiated the role of ultrasound in nerve evaluation in leprosy. The following observations were made

1. Age of the study population ranged from 20-46 years with mean age of 34.9 years.
2. Males and females in the study were in the ratio of 3:2.
3. The mean duration of symptoms in patients was 11.03 ±8 months with range of 2 to 24 months. Majority of them had symptoms for 2-6 months.
4. The nerve involvement was seen in all the patients.Majority of the patients (15 patients- 83.4%) had more than one nerve involvement.
5. The ulnar nerve (62%) was most frequently involved.
6. The sensory deficits were seen in 60% of patients, motor deficits in 7% , both motor and sensory deficits in 10%. The sensory modality was most frequently affected and much earlier than motor affection.

7. The clinical spectrum of patients were 14 Borderline tuberculoid form, 6 borderline lepromatous , 6 lepromatous form and 5 pure neuritic leprosy.
8. The reactions were observed in 6 patients with 4 type 1 reaction and 2 type 2 reaction.
9. On clinical palpation, 78 (32.5%) nerves out of 240 were thickened. Among which thirteen nerves were tender on palpation. Most nerves (40 nerves) showed grade 2 thickening followed by grade 1 (36 nerves).
10. For controls, the mean CSA for ulnar nerve was 7.2±1.1 mm^2 ,radial cutaneous nerve was 7.2±1.3 mm^2 , median nerve was 5.3±1 mm^2 ,lateral popliteal was 7.2±1.1 mm^2 , posterior tibial nerve was 6.3±0.5 mm^2 .
11. For cases, the mean CSA for ulnar nerve was 11.8 ±3.1mm^2 ,radial cutaneous nerve was 8.1±2.0 mm^2 , median nerve was 5.6 ±2.8 mm^2 , lateral popliteal was 8.9 ±3.3mm^2 , posterior tibial nerve was 7.7 ±3.5mm^2 .
12. The mean CSA of all nerves of leprosy patients were higher than that of controls. (**p value** for ulnar <0.005, radial cutaneous <0.025)
13. The echotexture of nerves in controls showed normoechogenicity in all nerves. In patients, 40.6% of the nerves showed hypoechogenicity

and 59.3% were normoechoic. The ulnar nerve showed more echotextural changes than other nerves.

14. The colour Doppler flow in nerves were absent in controls. In patients group, 13 nerves in 7 patients showed increased vascularity in the nerves which was correlated with inflammation of the nerves.
15. Increased vascularity was also observed in patients with impending reaction .
16. Correlation between clinical thickness of nerves and ultrasound parameters were statistically significant. For CSA and Echotexture, p value siginificant at <0.05 level for ulnar, radial cutaneous, posterior tibial and lateral popliteal nerves.

CONCLUSION

On the basis of the findings of the study with High Resolution Ultrasonography (HRUS), the following recommendations may be suggested:

- High resolution sonography of nerves is superior than clinical palpation of nerves with lesser interobserver variability. The nerves located deeper can be assessed which was not made out on clinical palpation.
- HRUS provides an objective way of measuring structural changes of the nerve and its damage. It also assesses the tissues surrounding the peripheral nerve.
- It helps in locating nerve abscess along the course of nerve and guides to drain it.
- It also helps in doing Fine needle aspiration cytology of nerve at suspected site in the diagnosis of pure neuritic leprosy.
- The intraneural edema occurring in reactions increases the cross sectional area of the nerve which could be measured on ultrasound precisely. This could be utilised for follow up of patients with reactions.
- Colour Doppler examination shows increased vascularity in the nerves in reactions. Thus, it can be used in follow up for the patients

with reactions. Increased vascularity is also observed in early reactions which enable to start steroid therapy early to prevent further nerve damage.

- HRUS examination has many advantages in imaging the peripheral nerves of leprosy. It is non-invasive in evaluating structural changes of the nerve that cannot be biopsied for histopathological examination.

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INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

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Telephone No.044 25305301
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CERTIFICATE OF APPROVAL

To
Dr.Bala Soundar.V.
PG in MD(DVL)
Madras Medical College/RGGGH
Chennai 600 003

Dear Dr.Bala Soundar.V.,

The Institutional Ethics Committee has considered your request and approved your study titled **"ROLE OF HIGH RESOLUTION ULTRASONOGRAPHY OF PERIPHERAL NERVES IN LEPROSY PATIENTS" - NO.03012016.**

The following members of Ethics Committee were present in the meeting hold on **12.01.2016** conducted at Madras Medical College, Chennai 3

1.Dr.C.Rajendran, MD.,	:Chairperson
2.Dr.R.Vimala,MD.,Dean,MMC,Ch-3	:Deputy Chairperson
3.Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	: Member Secretary
4.Prof.B.Vasanthi,MD.,Inst.of Pharmacology,MMC,Ch-3	: Member
5.Prof.P.Raghumani,MS, Dept.of Surgery,RGGGH,Ch-3	: Member
6.Prof.M.Saraswathi,MD.,Director, Inst.of Path,MMC,Ch-3	: Member
7.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person
8.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
9.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

MADRAS MEDICAL COLLEGE
21 JAN 2016
CHENNAI-600 003

Member Secretary – Ethics Committee
MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

PROFORMA

Case No :

PATIENT DETAILS:

Name : Age : Sex: OP No :

Address : Occupation :

Main Complaints:

H/O present illness;

- Duration of illness
- Sites involved
- Progression

H/O hypopigmentedanaesthetic lesions

H/O difficulty in combing hair,buttoning the shirt

H/O difficulty in holding slippers

H/O sensory loss over any areas

H/O cranial nerve palsies

H/O fever,joint pain

H/O drug intake

H/O treatment for similar illness in the past

H/O any other systemic illness

H/O visual disturbances

H/O any drug allergy

H/O trophic ulcer

H/O deformity

Associated dermatological disorders:

Past history:

H/O similar illness in the past

H/O any other comorbid illness

Family history:

Similar illness in other family member**s**

Treatment history:

Personal history:

Diet

Alcoholic

Smoking

CLINICAL EXAMINATION:

General examination :

Generalizedlymphadenopathy

Pulse : /min BP : / mm of Hg RR : /min Temp :

Pallor : Icterus :

CVS :

RS :

P/A :

CNS:

Bones and joints:

DERMATOLOGICAL EXAMINATION:

- Morphology of lesion :
- Distribution :
- Sensation :

Motor system:

Sensory system:

Examination of peripheral nerves:

Trophic changes

Gait

Palms and soles:

Oral and genital Mucosa:

Hair and nail:

INVESTIGATIONS:

1. Routine blood investigations

   Complete blood count

   RFT

   LFT
2. Slit skin smear for Acid Fast Bacilli
3. Skin biopsy
4. Nerve conduction study
5. Ultrasonogram of peripheral nerves

   Colour Doppler of nerves

TREATMENT :

FOLLOW UP:

ULTRASONOGRAM REPORT

PATIENT DETAILS:

Name : Age/Sex : OP No :

Address : Occupation : Date:

ULTRASONOGRAM FINDINGS:

	LEFT	RIGHT
ULNAR NERVE • CSA • Thickness at Elbow • Texture		
MEDIAN NERVE • CSA • Thickness at Wrist • Texture		
RADIAL NERVE • CSA • Thickness at wrist		
POSTERIOR TIBIAL NERVE • CSA • Thickness at		
LATERAL POPLITEAL NERVE • CSA • Thickness at		

COLOUR DOPPLER FINDINGS:

	LEFT	RIGHT
ULNAR NERVE		
MEDIAN NERVE		
RADIAL CUTANEOUS		
LATERAL POPLITEAL		
POSTERIOR TIBIAL		

INFORMATION SHEET

Name of Investigator: Dr.BalaSoundar.V

Name of Participant :

Title :**ROLE OF HIGH RESOLUTION ULTRASONOGRAPHY OF PERIPHERAL NERVES IN LEPROSY PATIENTS**

You are invited to take part in this study. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

We are conducting a study on:

ROLE OF HIGH RESOLUTION ULTRASONOGRAPHY OF PERIPHERAL NERVES IN LEPROSY PATIENTSamong patients attending Hansen OPD in our Rajiv Gandhi Government General Hospital, Chennai.

- Your participation may be valuable to us.
- The purpose of the study is to determine the sonographic findings of peripheral nerves in newly diagnosed leprosy patients.
- We will take detailed history and clinical examination. we will do blood investigations and slit skin smear.If needed we will obtain a small piece

of skin to do biopsy for confimation of diagnosis in suspicious cases. Nerve conduction studies will be done in selected cases.We will do ultrasonogram and colour Doppler of peripheral nerves.

- This study will not affect your treatment.
- Your privacy in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.
- Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.
- The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Date:Signature of investigator Signature of participant

PATIENT CONSENT FORM

Title of the study :: ROLE OF HIGH RESOLUTION ULTRASONOGRAPHY OF PERIPHERAL NERVES IN LEPROSY PATIENTS

Name of the Participant :

Name of the Principal Investigator : Dr. V.BALA SOUNDAR

Name of the Institution : Department of Dermatology & Leprosy,

Rajiv Gandhi Government General Hospital,

Chennai

Documentation of the Informed Consent :

I _____ have read/it has been read for me, the information in this form. I was free to ask any questions and they have been answered. I am over 18 years of age and exercising my free power of choice, hereby give my consent to be included as a participant in the study.

1. I have read and understood this consent form and the information provided to me.
2. I have had the consent document explained in detail to me.
3. I have been explained about the nature of my study.

4. My rights and responsibilities have been explained to me by the investigator.
5. I agree to cooperate with the investigator and I will inform her immediately if I suffer from unusual symptoms.
6. I have not participated in any research study at any time.
7. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.
8. I hereby give permission to the investigators to release the information obtained from me as a result of participation in this study to the regulatory authorities, government agencies, and Institutional Ethics Committee. I understand that they are publicly presented.
9. My identity will be kept confidential if my data are publicly presented.
10. I am aware that if I have any question during this study, I should contact the concerned investigator

Participant's Initials : _____

For adult participants:

Name and signature/thumb impression of the participant (or legal representative if participant incompetent)

_____ _____ _____

Name Signature Date

Name and signature of impartial witness (required for illiterate patients)

_____	_____	_____
Name	Signature	Date

Address and contact number of the impartial witness :

Name and signature of the investigator or his representative obtaining consent:

_____	_____	_____
Name	Signature	Date

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராய்ச்சியின் தலைப்பு :

தொழுநோயாளிகளின் நரம்புகளை ஆராய்வதில் மீயொலி (அல்ட்ரா சவுண்ட் ஸ்கேன்) நோட்டத்தின் பங்கு குறித்த ஆய்வு.

ஆராய்ச்சி செய்பவரின் பெயர் : மருத்துவர். வீ.பாலசௌந்தர்

ஆராய்ச்சி மையம் : ராஜீவ் காந்தி அரசு பொது மருத்துவமனை
சென்னை-600003.

பங்கேற்பாளர் பெயர் : வயது : பாலினம் :

..... எனும் நான், எனக்கு கொடுத்துள்ள தகவல் தாளைப் படித்து புரிந்து கொண்டேன். நான் பதினெட்டு வயதைத் கடந்துள்ளதால், என்னுடைய சுயநினைவுடனும், முழு சுதந்திரத்துடனும், இந்த ஆராய்ச்சியில் என்னை சேர்த்துக் கொள்ள சம்மதிக்கிறேன்.

1. நான் எனக்கு அளிக்கப்பட்ட ஒப்புதல் படிவத்தையும், தகவல்களையும் படித்து புரிந்து கொண்டேன்.
2. ஒப்புதல் படிவத்தில் உள்ள தகவல்கள் எனக்கு விளக்கிக் கூறப்பட்டன.
3. ஆய்வின் தன்மை பற்றி எனக்கு விளக்கப்பட்டது.
4. என்னுடைய உரிமைகளையும், பொறுப்புகளையும் ஆராய்ச்சியாளர் விளக்கிக் கூறினார்.
5. நான் இதுவரை எடுத்துள்ள / எடுத்து கொண்டிருக்கும் அனைத்து விதமான சிகிச்சை முறைகளையும் ஆராய்ச்சியாளரிடம் கூறியுள்ளேன்.
6. இந்த ஆராய்ச்சியினால் ஏற்படும் தீமைகள் பற்றி விளக்கப்பட்டன.
7. நான் ஆராய்ச்சியாளருடன் ஒத்துழைப்பேன் என்றும் எனக்கு ஏற்படக்கூடிய அசாதாரணமான நிகழ்வுகள் பற்றியும் உடனடியாக ஆராய்ச்சியாளரிடம் தெரிவிப்பேன் என்றும் உறுதி கூறுகிறேன்.
8. நான் க்டந்த ..... மாதங்களாக எந்தவிதமான ஆய்வுகளிலும் பங்கேற்கவில்லை.
9. எனக்கு செய்யப்படும் அனைத்து பரிசோதனைகளும் (உதாரணம் : இரத்தம் எடுத்தல்) என் நோயின் தன்மையை அறிவதற்காக செய்யப்படுபவை என்பதை அறிகிறேன்.

10. இந்த ஆய்விலிருந்து எப்போது வேண்டுமானாலும் எக்காரணமும் கூறாமல் நான் என்னை விடுவித்துக் கொள்ளலாம் என்பதை அறிவேன் மற்றும் இதனால் எனக்குத் தரப்படும் சிகிச்சைக்கு எந்த பாதிப்பும் வராது என்பதை அறிவேன்.

11. ஆராய்ச்சியாளர்கள் இந்த ஆய்வில் எனது பங்களிப்பை எந்த நேரத்திலும் எக்காரணமும் கூறாமல் என் சம்மதம் இல்லாமலும் என்னை விலக்கிவிட முடியும் என்பதை அறிவேன்.

12. என்னிடம் இருந்து பெறப்படும் தகவல்களை அரசு, வரைமுறை அதிகாரிகள் ஆகியோர்களுடன் பகிர்ந்து கொள்ள ஆராய்ச்சியாளர்களுக்கு அனுமதி அளிக்கிறேன். என்னுடைய தஸ்தாவேஜுகளை பார்வையிட அவர்களுக்கு உரிமை உண்டு.

13. என்னிடம் பெறப்படும் தகவல்கள் பொதுவாக பரிசுரிக்கப்பட்டாலும், என்னுடைய அடையாளம் இரகசியமாக வைக்கப்படும் என்பதை அறிவேன்.

14. எனக்கு திருப்தி அளிக்கும் வகையில் என்னிடம் கேட்கப்பட்ட கேள்விகளுக்கு நான் பதில் அளித்துள்ளேன்.

15. இந்த ஆராய்ச்சியில் பங்கேற்க தன்னிச்சையாக முழுமனதுடன் நான் சம்மதிக்கிறேன்.

இந்த ஆய்வின் போது எனக்கு என்ன சந்தேகம் ஏற்பட்டாலும் ஆராய்ச்சியாளரை தொடர்பு கொள்ளலாம் என்பதை அறிவேன்.

இந்த ஒப்புதல் படிவத்தில் கையெழுத்திடுவதன் மூலம் இங்கு தரப்பட்டிருக்கும் அனைத்து தகவல்களும் தெளிவாகக் கூறப்பட்டு என்னால் முழுமையாக புரிந்து கொள்ளப்பட்டது என்பதை சான்றளிக்கிறேன். இந்த ஒப்புதல் படிவத்தின் நகல் என்னால் பெற்றுக் கொள்ளப்பட்டது.

பங்கேற்பவரின் கையொப்பம் இடம் :

கட்டைவிரல் ரேகை : தேதி :

பங்கேற்பவரின் பெயர் :
விலாசம் :

ஆய்வாளரின் பெயர் : இடம் :

தேதி :

ஆய்வு தகவல் தாள்

ஆராய்ச்சியின் தலைப்பு :

தொழுநோயாளிகளின் நரம்புகளை ஆராய்வதில் மீயொலி (அல்ட்ரா சவுண்ட் ஸ்கேன்) நோட்டத்தின் பங்கு குறித்த ஆய்வு.

ஆய்வாளர் :

பங்கேற்பாளர் : **வயது :** **பாலினம் :**

ஆராய்ச்சி மையம் : **தோல் நோய் துறை, இராஜீவ் காந்தி அரசு பொது மருத்துவமனை, சென்னை.**

இந்த ஆய்வில் பங்கேற்பதற்காக தாங்கள் அழைக்கப்படுகிறீர்கள். இந்த ஆவணத்தில் உள்ள தகவல்கள் தாங்கள் இந்த ஆய்வில் பங்கேற்க முடிவு செய்துக் கொள்ள உதவும். இதில் ஏதேனும் சந்தேகம் இருந்தால் வெளிப்படையாக கேள்விகளைக் கேட்டு தெரிந்துக் கொள்ளலாம்.

நாங்கள் இராஜீவ் காந்தி அரசு பொது மருத்துவமனையில் தொழுநோயினால் நரம்புகளில் ஏற்படக்கூடிய மாற்றங்களை மீயொலி நோட்டம் மூலம் அறிந்துக் கொள்வதற்கான ஆய்வை நடத்துகிறோம்.

அதற்கு உங்கள் பங்களிப்பு எங்களுக்கு பெரிதும் உதவக்கூடும்.

இந்த ஆய்வின் நோக்கம்:

தென்னிந்தியாவின் இப்பகுதியில் உள்ள இம்மருத்துவக் கல்லூரி மருத்துவமனைக்கு வரும் நோயாளிகளிடம் தொழுநோயினால் நரம்புகளின் மாற்றங்களை அறிந்துக் கொள்வதற்கான ஆய்வாகும்.

இவ்வாராய்ச்சியில் தங்களிடையே அடிப்படை மற்றும் தொழுநோய் குறித்த விரிவான கேள்விகள் கேட்கப்படும். பின்னர் நீங்கள் மருத்துவப் பரிசோதனைக்கு உட்படுத்தப்படுவீர்கள். அனைவரிடமும் இரத்த மாதிரி பெறப்பட்டு அது வழக்கமான இரத்தப் பரிசோதனைக்கும் (CBC, RFT, LFT) உபயோகப்படுத்தப்படும். தேவைப்படும் நபர்களுக்கு தோலில் லிக்னோகைன் மருந்து செலுத்தி திசு ஆய்வும், மேற்கொள்ளப்படும். இந்த ஆய்வில் அல்ட்ரா சவுண்ட் மூலம் நரம்புகளில் உள்ள மாற்றங்கள் கண்டறியப்படும்.

தங்களது மருத்துவ சிகிச்சை குறித்த தகவல்கள் இரகசியமாக பாதுகாக்கப்படும். ஆய்வின் போதோ அல்லது முடிவுகளை வெளியிடும் போதோ தங்களது பெயரையோ, அடையாளங்களையோ வெளியிடமாட்டோம் என்பதை தெரிவித்துக் கொள்கிறோம்.

இந்த ஆய்வில் பங்கேற்பது உங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆய்விலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம். இந்த ஆய்வில் பங்கேற்காவிட்டாலும் நீங்கள் வழக்கமான சிகிச்சையை தொடர்ந்து பெறலாம்.

இந்த ஆய்வின் முடிவு தங்களுக்கு ஆய்வின் இறுதியிலோ அல்லது ஆய்வின் போதிலோ தெரியப்படுத்தப்படும்.

ஆய்வாளர் கையொப்பம்

பங்கேற்பாளர் / பாதுகாவலர் கையொப்பம்

தேதி :


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Dissertation Submitted in
Partial fulfillment of the University regulations for
MD DEGREE IN
DERMATOLOGY, VENEREOLOGY AND LEPROSY
(BRANCH XX)
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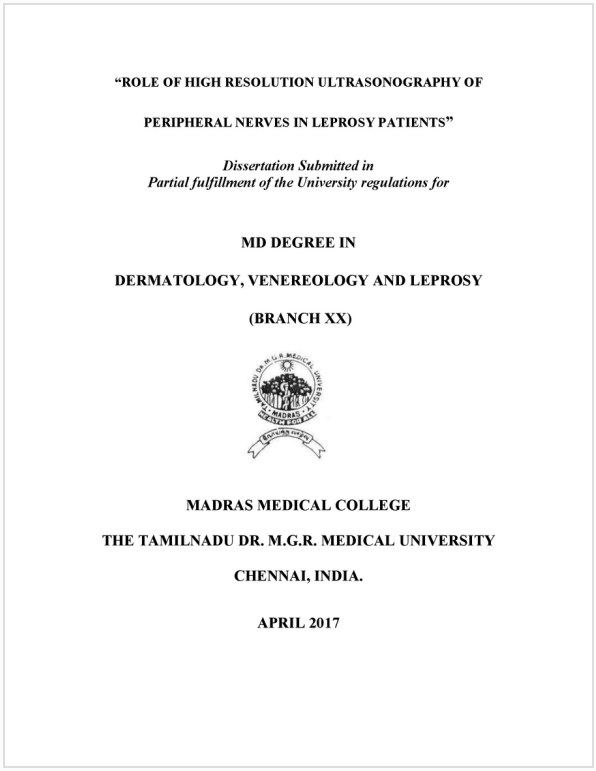

"ROLE OF HIGH RESOLUTION ULTRASONOGRAPHY OF

PERIPHERAL NERVES IN LEPROSY PATIENTS"

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(BRANCH XX)

MADRAS MEDICAL COLLEGE

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI, INDIA.

APRIL 2017

S.N	NAME	AGE	SEX	OCCUPATION	Duration of symptoms(months)	NUMBER OF PATCHES	NUMBER OF NERVES INVOLVED	MOTOR DEFICITS	SENSORY DEFICITS	SPECTRUM	REACTION	CLINICAL NERVE GRADING-THICKNESS										CLINICAL NERV			
												RIGHT					LEFT					RIGHT			
												UN	RN	MN	LPN	PTN	UN	RN	MN	LPN	PTN	UN	RN	MN	LPN
1	Rajeshwaran	25	M	STUDENT	12	4	1	N	Y	BT	N	1	0	0	0	0	0	0	0	0	0	0	0	0	0
2	Mani	40	M	LABOURER	24	34	4	N	Y	LL	N	2	0	0	2	0	2	0	0	2	0	0	0	0	0
3	Murugan	45	M	LABOURER	2	0	2	Y	Y	PNL	N	0	0	0	0	2	0	0	0	0	2	0	0	0	0
4	Uma Maheswari	27	F	HOUSEWIF	6	0	4	N	Y	PNL	N	2	0	0	2	0	2	0	0	1	0	0	0	0	0
5	Selvam	32	M	LABOURER	12	20	4	N	Y	LL	Y	2	0	0	1	0	2	0	0	1	0	2	0	0	1
6	Sadasivam	29	M	LABOURER	3	0	5	Y	Y	PNL	N	1	0	0	2	1	0	0	0	2	1	0	0	0	0
7	Mukesh Kumar	45	M	PROFESSIO	5	0	3	N	Y	PNL	N	0	0	0	2	1	1	0	0	0	0	0	0	0	0
8	Rajan	29	M	LABOURER	3	3	1	N	Y	BT	Y	0	0	0	0	0	1	0	0	0	0	0	1	0	0
9	Ragavan	42	M	LABOURER	6	12	2	N	N	BL	Y	2	1	0	0	0	0	0	0	0	0	2	1	0	0
10	Bakthavatsalam	32	M	LABOURER	2	2	1	N	Y	BT	N	1	0	0	0	0	0	0	0	0	0	0	0	0	0
11	Jayapaul	36	M	LABOURER	3	20	2	N	Y	BL	N	1	0	0	0	1	0	0	0	1	0	0	0	0	0
12	Manavalan	44	M	LABOURER	5	7	1	Y	Y	BT	N	2	0	0	0	0	0	0	0	0	0	0	0	0	0
13	Sumathy	35	F	HOUSEWIF	24	4	1	N	N	BT	Y	1	0	0	0	0	0	0	0	0	0	1	0	0	0
14	Navaneetham	46	F	HOUSEWIF	12	0	3	N	Y	PNL	N	0	0	0	2	2	0	0	0	2	0	0	0	0	0
15	Jayalakshmi	43	F	HOUSEWIF	5	15	2	N	Y	BL	Y	0	0	0	1	0	0	0	0	1	0	0	0	0	1
16	Kaliyaperumal	45	M	DRIVER	24	32	4	N	Y	LL	N	3	1	0	1	0	3	0	0	0	0	0	0	0	0
17	Selvaraj	28	M	LABOURER	8	6	2	N	N	BT	Y	2	0	0	0	0	0	0	0	1	0	1	0	0	0
18	Meera	27	F	LABOURER	16	4	2	N	N	BT	N	2	0	0	0	0	0	1	0	0	0	0	0	0	0
19	Jayanthi	46	F	LABOURER	6	4	2	N	Y	BT	N	2	0	0	0	0	2	0	0	0	0	0	0	0	0
20	Selvi	45	F	HOUSEWIF	12	28	4	N	Y	LL	N	2	0	0	2	0	2	0	0	2	0	0	0	0	0
21	Rani	35	F	HOUSEWIF	12	6	2	N	N	BT	N	0	0	0	2	0	0	0	0	0	1	0	0	0	0
22	Bharath	20	M	STUDENT	12	20	3	N	N	BL	N	2	1	0	0	0	2	0	0	0	0	0	0	0	0
23	Sarojammal	45	F	HOUSEWIF	24	23	4	N	N	BL	N	2	1	0	0	0	2	0	0	1	0	0	0	0	0
24	vanaja	23	F	HOUSEWIF	3	2	2	N	N	BT	N	1	0	0	0	0	0	1	0	0	0	0	0	0	0
25	Padmavathy	42	F	HOUSEWIF	12	4	2	N	Y	BT	N	1	0	0	0	0	0	1	0	0	0	0	0	0	0
26	Puroshathaman	23	M	STUDENT	4	5	2	N	Y	BT	N	2	0	0	0	0	2	0	0	0	0	0	0	0	0
27	Senthil Kumar	33	M	DRIVER	15	4	2	N	Y	BT	N	1	0	0	0	0	0	1	0	0	0	0	0	0	0
28	Amudha	32	F	HOUSEWIF	12	35	4	N	Y	LL	N	2	0	0	2	0	2	0	0	1	0	0	0	0	0
29	Raveendra Kumar	30	M	DRIVER	24	24	4	N	Y	BL	N	2	0	0	0	0	2	0	0	1	1	0	0	0	0
30	Aravind	24	M	STUDENT	6	6	2	N	N	BT	N	2	0	0	0	0	0	0	0	1	0	0	0	0	0

/E GRADING -TENDERNESS						CROSS SECTIONAL AREA (mm2)										TEXTURE										COLOUR DOPPLER FLOW									
	LEFT					RIGHT					LEFT					RIGHT					LEFT					RIGHT					LEFT				
PTN	UN	RN	MN	LPN	PTN	UN	RN	MN	LPN	PTN	UN	RN	MN	LPN	PTN	UN	RN	MN	LPN	PTN	UN	RN	MN	LPN	PTN	UN	RN	MN	LPN	PTN	UN	RN	MN	LPN	PTN
0	0	0	0	0	0	12.20	8.3	4.9	5.2	5.3	10.4	8.1	4.8	5.1	5.2	2	0	0	0	0	1	0	0	0	0	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	15.70	8.5	12.2	16	9.4	14.5	8.3	11.9	16	6.8	2	0	1	1	1	3	0	0	0	0	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	12.4	10.2	6.4	8.6	12.8	12.2	10.4	6.2	8.4	12.6	0	0	0	0	1	0	0	0	1	1	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	15.4	6	6.3	16	7.5	18.4	6.4	12	15.4	7.8	1	0	1	2	0	1	0	0	1	0	N	N	N	N	N	N	N	N	N	N
0	2	0	0	1	0	16.8	10	5.6	10	7.4	18.4	9.6	5.4	7.5	7.2	2	0	1	1	0	2	0	1	1	0	Y	N	N	Y	N	Y	N	N	Y	N
0	0	0	0	0	0	10	8.8	4.8	15	9.4	8.7	4.2	13.6	9.8	6.6	1	0	0	1	1	1	0	1	1	1	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	8	6.1	4.4	14	10.6	10.6	6.8	3.8	6.5	6.1	0	0	0	1	1	1	0	1	0	1	N	N	N	N	N	N	N	N	N	N
0	2	0	0	0	0	8.6	7.2	5.3	6.1	7	16.8	7.2	5.9	8.6	8	0	0	1	0	1	1	0	0	1	0	Y	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	13.6	11.8	4.9	6.6	6.9	11.9	8.9	4.8	6.2	5.6	1	1	0	1	0	1	1	1	1	0	Y	Y	N	N	Y	Y	N	N	N	N
0	0	0	0	0	0	10.2	8.2	4.8	5.4	5.2	9.2	7.8	4.4	5.2	5	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	5.4	4.4	4.2	5.8	10.9	5.2	4.2	3.8	10.2	10.5	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	14.2	5.2	3.5	5.2	4.8	10	4.8	3.7	4.8	4.6	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	12.5	8.1	6.4	7.1	6.2	7.3	7.8	6.6	7	6.6	0	0	0	0	0	0	0	0	0	0	Y	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	7.2	8.2	5.6	12	13.4	7	8.1	5.4	12.2	6.4	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
0	0	0	0	1	0	7.3	7.2	3.2	9.6	5.1	7	7	3	10.6	4.9	1	0	0	2	1	1	0	0	2	1	N	N	N	Y	N	N	N	N	Y	N
0	0	0	0	0	0	15.1	11	3.8	10	8.2	16	8	3.4	8.2	7.8	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
0	0	0	1	0	0	12.8	8.4	4.8	9.2	6.4	9.6	8.1	4.5	9.6	8	0	0	0	0	0	0	0	0	0	0	Y	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	13.8	10.2	7.6	5.8	5.4	8.2	13.2	7.8	5.4	5.6	2	0	1	0	1	1	0	1	0	0	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	13.4	8.2	4.8	6.8	6.4	13.4	8	4.6	6.6	6.2	2	0	1	0	1	2	0	1	1	0	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	13.8	9.4	5.4	15	8.4	14.2	9.2	5.2	14.2	8.2	1	1	0	2	1	1	1	0	0	1	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	7.4	6	5.8	16	13	7.8	7.3	5	12.6	15.6	0	0	1	2	0	1	0	0	1	1	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	13.4	11.4	4.1	5.8	5.4	13.2	10	3.6	5.6	5.2	2	1	0	1	0	2	0	1	0	0	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	13.2	12.2	5.4	6.8	6.4	12.8	9.2	4.2	10.2	6.2	2	1	0	1	0	2	1	1	0	1	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	9.2	5.1	6.4	5.3	5.1	10.3	5	6	6.1	5.6	1	0	1	0	0	1	1	0	1	0	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	11.2	8.6	4.8	6.4	6.4	8.1	11.4	4.6	6.2	6.2	1	0	1	0	0	1	0	0	1	1	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	14	8.1	5.3	6.3	8	13.8	8.8	5.6	6.1	7.5	2	0	0	1	0	2	1	0	1	0	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	10.3	8.1	5.6	7	6.2	9.4	9	6.4	6.8	5.6	1	0	0	1	0	1	1	0	1	0	Y	N	N	N	N	Y	N	N	N	N
0	0	0	0	0	0	11.4	5.9	6.8	8.3	6.6	10.8	5.7	7	10.4	6	2	0	1	2	0	2	0	1	1	0	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	14.5	9.3	5.1	6.5	8.8	10.4	9.6	5.3	7.8	9.1	2	0	1	0	0	2	1	0	1	1	N	N	N	N	N	N	N	N	N	N
0	0	0	0	0	0	12.4	9.4	6	9.2	7.1	9	9.2	6.8	10.4	8.1	2	0	1	0	1	1	0	0	1	0	N	N	N	N	N	N	N	N	N	N

S.N	Name	AGE	SEX	OCCUPATION	CROSS SECTIONAL AREA (in mm2)										TEXTURE - Normo/ hypoechoic										COLOUR DOPPLER									
					RIGHT					LEFT					RIGHT					LEFT					RIGHT				LEFT					
					UN	RN	MN	LPN	PTN	UN	RN	MN	LPN	PTN	UN	RN	MN	LPN	PTN	UN	RN	MN	LPN	PTN	UN	RN	MN	LPN	PTN	UN	RN	MN	LPN	PTN
1	Adhithya	20	M	Student	6.3	6.1	6.5	7.8	5.2	6.2	6	6.7	7.3	5.1	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
2	Arul	44	M	Professional	6.8	6.5	4.6	6.5	6.4	6.4	6.3	4.7	6.3	6.4	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
3	Arun	32	M	Manual labourer	6.7	7	5.4	7.2	5.8	6.9	6.8	5.7	6.8	5.8	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
4	Ashwin	25	M	Professional	7.4	6	5.9	5.9	6.7	7.2	5.7	5.5	5.7	6.7	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
5	Banu	35	F	Manual labourer	6.4	7.1	5.4	8.6	7.2	6.7	6.2	5.2	8.3	7.2	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
6	Dhinakar	45	M	Professional	8.5	6.9	4.6	7.9	5.7	8.4	5.7	4.7	7.9	5.7	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
7	Kalaiarasan	29	M	Manual labourer	6.7	10	4.5	5.8	7.8	6.9	9.8	4.3	5.6	7.8	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
8	Keerthi	27	F	Housewife	9.3	10	4.7	8.4	7.5	9.1	9.3	4.5	8.2	7.5	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
9	Lavanya	35	F	Housewife	5.3	9.1	3.6	8.6	6.4	5.1	8.9	3.7	8.3	6.4	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
10	Mahesh	28	M	Manual labourer	7.8	14	5.2	8.6	5.6	8.1	12	5	8.6	5.6	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
11	Malathy	32	F	Housewife	4.5	7	5.8	6.5	7.5	4.7	6.2	5.3	5.5	7.5	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
12	Mohan	36	M	Professional	6.5	8	3.5	5.7	7.6	6.9	8.7	3.7	5.6	7.6	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
13	Murugan	45	M	Manual labourer	7.2	6.5	6.2	9.4	5.6	7.1	5.5	6.1	8.6	5.6	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
14	Nithya	23	F	Housewife	7.8	7.2	5.6	9.1	6.7	7.6	7.2	5.4	9.2	6.7	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
15	Ponni	46	F	Manual labourer	7.5	8.2	4.6	7.4	6.3	7.3	8	4.5	7.2	6.1	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
16	Prakash	40	M	Manual labourer	7.8	8.1	4.6	6.8	5.3	7.4	7.7	4.3	6.5	5.3	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
17	Prem	32	M	Manual labourer	8.1	5.9	5.6	6.9	6.4	8	6	5.4	6.7	6.4	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
18	Ranjith	29	M	Manual labourer	8.5	8.5	5.2	8.6	6.3	8.2	8.5	4.9	8.2	6.3	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
19	Ravi	42	M	Manual labourer	8.2	6.1	5.6	8.5	5.9	7.9	6.3	5.2	7.8	5.9	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
20	Rekha	43	F	Housewife	6.4	7	5.7	7.5	6.1	6.6	7.2	5.4	7.2	6.2	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
21	Saranya	27	F	Housewife	4.9	7.4	4.5	7.8	5.7	7.8	7.2	4.3	7.8	5.7	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
22	Saravana Kumar	45	M	Professional	5.2	4.5	4.3	5.5	6.8	5.4	5.5	4.7	5.5	6.8	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N

23	Sasikala	46	F	Housewife	7.4	6.4	6.4	8.3	7.3	7.6	6.6	6.5	8.1	7.3	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
24	Sathish	33	M	Professional	9.8	5.3	5.3	8.4	7.5	7.8	6.3	5.6	8.4	7.8	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
25	selvi	45	F	Housewife	8.5	6.8	5.7	5.7	5.6	8.1	6.2	5.4	5.7	5.6	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
26	Sudharshan	23	M	Manual labourer	7.6	7.1	6.2	6.4	7.5	7.4	8.4	6	6.2	7.6	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
27	Suresh	24	M	Manual labourer	9.8	6.1	7.5	5.9	6.9	9.6	5.7	7.3	5.8	6.9	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
28	Vanitha	42	F	Manual labourer	7.6	8.1	4.6	7.4	5.8	7.4	9	4.5	7.2	5.8	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
29	Velankanni	45	F	Housewife	7.4	8.1	5.4	7.5	5.8	7.6	8.8	5.5	7.3	5.8	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N
30	Vinoth	30	M	Professional	6.2	6.3	7.6	7.5	4.9	6.4	6.3	7.4	7.3	4.9	0	0	0	0	0	0	0	0	0	0	N	N	N	N	N	N	N	N	N	N

CODING AND KEY FOR MASTER CHART

UN –Ulnar nerve

RN- Radial cutaneous nerve

MN- Median nerve

LPN – Lateral popliteal nerve

PTN – Posterior Tibial nerve

CSA – Cross sectional area

BT - Borderline tuberculoid

BB - Borderline borderline

BL - Borderline lepromatous

LL - Lepromatous leprosy

PNL – Pure Neuritic Leprosy

Key :

1. Motor deficits and Sensory deficits –

   Y – Present

   N – Absent

2. Reaction –

   Y – Present

   N – Absent

3. Thickness grading –

   0- Normal

   1- Mild

   2- Moderate

   3- Severe

4. Texture of nerve

   0- Normal

   1- Mild hypoechoic

   2- Obvious hypoechoic

   3- Severe loss of fascicular pattern

5. Colour Doppler

   Y –Flow present

   N - FlowAbsent